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U. S. DEPARTMENT OF AGRICULTURE,
BUREAU OF ANIMAL INDUSTRY—Bulletin No. 52, Part II
D. E. SALMON, D. V. M., Chief of Bureau.

EXPERIMENTS CONCERNING TUBERCULOSIS,

UNDER THE SUPERVISION OF

THE BIOCHEMIC DIVISION.

PART II.

The Comparative Virulence of Human and Bovine Tubercle Bacilli for Some Large Animals.

BY

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1905.

LETTER OF TRANSMITTAL.

U. S. Department of Agriculture,
Bureau of Animal Industry,
Washington, D. C., November 28, 1904.

Sir: I have the honor to transmit herewith a manuscript entitled "The comparative virulence of human and bovine tubercle bacilli for some large animals," by Drs. E. A. de Schweinitz, M. Dorset, and E. C. Schroeder.

When the experimental work described in this manuscript had been practically completed, Doctor de Schweinitz, who was at that time chief of the Biochemic Division of this Bureau, was taken suddenly ill and, to our great sorrow, died. This unfortunate occurrence threw upon the remaining authors of this paper the entire burden of its preparation, together with the formulation of the conclusions expressed therein. In view of this fact Doctor de Schweinitz should be given credit for the active part taken by him in the prosecution of these experiments, but should not be held responsible for the conclusions drawn therefrom.

This manuscript describes the inoculation of cattle, hogs, and monkeys with tuberculous virus of both human and bovine origin and bears directly upon the very important question of the infectiousness of bovine tuberculosis for human beings. I recommend that this manuscript, together with the accompanying illustrations, which are necessary to a thorough understanding of the text, be published as Part II of Bulletin No. 52 of this Bureau.

Respectfully,

D. E. Salmon,
Chief of Bureau.

Hon. James Wilson,
Secretary of Agriculture

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Part II.—THE COMPARATIVE VIRULENCE OF HUMAN AND BOVINE TUBERCLE BACILLI FOR SOME LARGE ANIMALS.

By E. A. DE SCHWEINITZ, PH. D., M. D., MARION DORSET, M. D., AND E. C. SCHROEDER, M. D. V.

The experiments described in this part of Bulletin No. 52 deal almost exclusively with (1) the infectiousness of tubercle bacilli of human origin for hogs and cattle and (2) the comparative virulence of human and bovine tuberculous virus for monkeys. The preliminary notes, indicating the important features of these experiments, have already been published, and it is our desire to present here the details of the experiments, together with a brief review of some of the literature which bears more or less directly upon the work we have done.

PLAN OF THE EXPERIMENTS.

The original plan adopted for these experiments contemplated the following lines of work:

(1) The isolation of fresh cultures of human tuberculosis from sputum and from cases of generalized tuberculosis in adults and children, obtaining whenever possible material from cases which indicated an involvement of the abdominal viscera.

(2) The inoculation of cattle and hogs intravenously and subcutaneously with the cultures or material so obtained.

(3) The feeding of human tuberculous material to calves.

(4) The isolation of fresh cultures of bovine tubercle bacilli and their use for comparison with the cultures from human beings mentioned above.

(5) The subcutaneous and intravenous inoculation of cattle and hogs with such bovine cultures or with bovine tuberculous material.

(6) The inoculation of cattle with bovine and human tubercle bacilli which had been under cultivation in the laboratory for some years and which possessed probably a comparatively low degree of virulence.

It was our plan to trace the histories of the subjects from whom the human tuberculous material was taken and to give complete autopsy records of these persons. The animals which succumbed to inoculation were to be carefully examined after death, and the lesions found were to be studied microscopically in order to determine if possible whether or not the disease produced was of a progressive character.

Before the experiments progressed very far it became evident that certain of the projected details which seemed quite desirable could not be fully carried out. The subjects from whom the tuberculous material was obtained belonged mostly to the pauper classes, and it was impossible to ascertain with any degree of certainty the sources of their food supply. In addition, the family histories were valueless almost without exception. In other cases from which sputum was obtained no autopsy was made when the subject finally died, owing usually to prejudice on the part of relatives. The records of most of the cases of human tuberculosis are therefore very unsatisfactory in so far as they concern the mode of infection.

But let it be remembered that the primary object of these experiments is to determine whether tuberculosis in cattle may be brought about by tubercle bacilli which have caused serious or fatal disease in man. The source from which the human beings were infected may be of great importance when it can be traced, but it is not necessary to a solution of the problem which we have undertaken.

METHOD OF OBTAINING THE CULTURES.

Before discussing the general features of the experiments it should be stated that all the cultures used were isolated from guinea pigs which had been inoculated with material from the various cases of human and bovine tuberculosis. As a rule, the cultures were obtained from the spleens of guinea pigs and grown on the egg medium, which is described in detail on page 9 of Part I of this bulletin. In the comparative inoculations the cultures were approximately of the same age and the doses given as nearly uniform as possible.

SOURCES OF HUMAN TUBERCULOUS MATERIAL.

As previously stated, we were unable to secure full data relative to the previous histories and autopsy conditions of many of the cases of human tuberculosis which supplied material for our investigations. In some instances the hospital records, although quite voluminous, were deficient in details of especial interest in experiments of this character; hence only such portions of them as have a direct bearing upon the origin or nature of the tuberculosis with which the several individuals were afflicted will be inserted in this bulletin.

We must express our sincere thanks to the physicians who kindly furnished us with material and records from the several hospitals in this city. The tissue obtained from the Government Hospital for the Insane was sent to us, together with the postmortem records, by

Dr. I. W. Blackburn, the pathologist of that institution. For the material from the Children's Hospital we are indebted to Doctors Grasty and Mason of the house staff, and for the sputum obtained from patients in the Washington Asylum Hospital to Doctor Price, house physician in the asylum.

(1) *Culture F T, human.*—This culture was obtained on egg from the lung of a guinea pig which had been inoculated intraabdominally with sputum from a 45-year-old negro woman whose occupation was that of a domestic. She was admitted to the Washington Asylum Hospital February 16, 1902, after a diagnosis of pulmonary tuberculosis with chronic interstitial nephritis had been made. There was nothing unusual during the course of her illness. She died February 23, 1902. No autopsy could be obtained.

(2) *Culture F L, human.*—This culture was obtained from the spleen of a guinea pig which had been inoculated intraperitoneally with sputum from a painter 40 years old. He was admitted to the Washington Asylum Hospital on June 26, 1902, after a diagnosis of pulmonary tuberculosis had been made. This patient died on November 4, 1902. Consent to a postmortem examination could not be obtained.

(3) *Culture S E No. 3, human.*—This culture was obtained from the spleen of a guinea pig which had been inoculated subcutaneously with a small fragment from the lung of a man 50 years old. This man was admitted to the Government Hospital for the Insane on July 28, 1890, suffering from chronic dementia. Owing to the patient's condition, no evidence could be obtained relative to his previous history. The illness which terminated in his death appeared to begin on September 3, 1901, when he had a chill followed by fever. From that date the temperature varied from 98° to 102° F. On May 15, 1902, the abdomen was distended and the patient vomited copiously. Death took place on May 16.

The autopsy revealed pleuritic adhesions of both lungs. In the left lung old tuberculous deposits were found; in the apex there were some small cavities; secondary tuberculous granulations were scattered throughout the remaining portion of the upper lobe and in patches throughout the lower lobe. In the right lung old tuberculous foci were found in the upper portion and tuberculous nodules throughout the remainder of the organ. The liver had undergone fatty degeneration; the intestines, large and small, were extensively ulcerated; the ulcerations were especially numerous in the small intestine. Many of the mesenteric glands were enormously enlarged, caseous, and some of them softened. A few tubercle bacilli were found in smear preparations from the granulations in the lung, but none could be demonstrated in the caseous material from the mesenteric glands.

(4) *Culture G D, human.*—This culture was obtained from the spleen of a guinea pig which had been inoculated with a small fragment of a peritoneal tubercle from a man 19 years old. The man was admitted to the Government Hospital for the Insane on February 11, 1902, suffering with acute mania associated with generalized tuberculosis. The tuberculosis apparently began about three months before admission to the hospital. The temperature ranged from 99° to 101.8° F. The sputum contained a very small number of tubercle bacilli. The patient gradually lost strength after admission, and died on May 7, 1902.

The autopsy revealed the following lesions: The lungs were adherent to the thoracic wall, except at the lower part of the left pleural cavity, where there was evidence of an old tuberculous empyema. Many miliary tubercles were scattered throughout both lungs but very few cavities were found. The bronchial glands were enlarged and caseous. The omentum, intestine, and all abdominal viscera were so bound together by inflammatory adhesions that it was impossible to remove any of the organs. The surface of the peritoneum was covered with yellowish white tuberculous masses ranging in size from a pin's head to one-fourth of an inch in diameter. The liver contained numerous tuberculous areas, some of which had broken down and produced cavities. The spleen was full of large tubercles; the kidneys showed numerous medium-sized tubercles. The intestines were matted together by adhesions and their mucous surface presented numerous small ulcers. There was also a tuberculous inflammation of the meninges of the brain. From the character of the disease it was impossible to determine accurately the mode of infection; it appeared probable, however, that the bronchial glands were the first of the internal organs to be involved, and it is not unlikely that the infection entered through the mouth or throat.

(5) *Culture No. 12,124, human.*—This culture was obtained from the spleen of a guinea pig which had been inoculated with a small fragment of the lung of a woman about 27 years of age. The woman was admitted to the Government Hospital for the Insane in November, 1900. She was an Indian, and was suffering from a form of congenital imbecility. She had lived the greater portion of her life in the woods, subsisting upon berries, game, and food which was voluntarily given to her. No detailed family history was obtainable. At the time of admission there was no suspicion of tuberculosis, but she began to fail shortly afterwards. She died on June 26, 1902.

The following synopsis of the postmortem lesions was kindly furnished us by Doctor Blackburn:

1. Tuberculous pleuritis, nodular, left side only. 2. Pulmonary tuberculosis with perforation. 3. Pneumothorax and pulmonary collapse. 4. Tuberculous ulceration of the intes-

tines. 5. Tuberculous lymphadenitis; mesenteric glands. 6. Tuberculous salpingitis with adhesions. 7. Perforation and localized peritonitis due to ulceration and adhesions of bowel in pelvic cavity. 8. Fatty infiltration of liver. 9. Moderate degree of interstitial nephritis. 10. Slight chronic lepto-meningitis and atrophy of brain. 11. Dilatation of left side of heart and cardiac thrombosis.

Remarks: The brief synopsis given shows the extent of distribution of the tuberculous lesions. The pulmonary disease seems to be ordinary acute phthisis. The pleural disease was unusual in that it was nodular and accompanied by active inflammation and was limited to one pleural cavity, the left. The nodules bore a considerable degree of resemblance to the pearl disease of cattle, a condition I do not often find. The intestinal ulcers were large and completely encircled the bowel. The primary seat of infection was probably the lungs.

(6) *Culture C No. 1, human.*—This culture was obtained from the spleen of a guinea pig which had been inoculated with a small fragment of a mesenteric gland from a child 19 months old. This child was admitted to the Children's Hospital on November 20, 1901. No family history could be obtained. The general history of the patient is as follows: A male child, fed partly at the breast and partly on cow's milk; had never enjoyed good health. On examination after admission to the hospital he was found to be markedly rachitic, and had a dull, apathetic expression. He was affected with a loose cough and his respiration was rapid and shallow. Mucous râles could be heard throughout the chest and some consolidation at the apex of the left lung was detected. The gastric and intestinal digestion was poor, but a physical examination of the abdomen failed to reveal anything abnormal. The patient gradually lost in condition from the time of his admission; appetite was and remained very poor, the pulse was rapid and weak, and he gradually passed into a moribund condition and died on December 22, 1901.

The autopsy record, which was kindly furnished us by Doctor Grasty, is as follows, the portions which have no direct bearing on tuberculosis being omitted:

Thorax: The diaphragm was adherent to the base of the right lung. There was a general adhesive pleurisy on this side with imperfect crepitation of the lung, which was mottled and grayish and studded with miliary tubercles which were especially numerous over the superior lobe and in the region of the apex. A cavity in the apex was about the size of a hazelnut. The left lung was consolidated at the apex. There was imperfect crepitation throughout the organ, and miliary tubercles from 1 to 5 mm. in size could be seen throughout the lung tissue. The lower lobe contained two large cavities filled with purulent material and threads of necrotic tissue. A microscopic examination of the contents of these cavities revealed the presence of many tubercle bacilli. The tracheobronchial glands were enlarged and caseous. Both pleuræ were studded with tubercles. The brain was congested and at its base some tubercles and a serous exudate were found. There were also tubercles in the cerebellum and fourth ventricle. In the abdominal cavity the liver was enlarged and mottled but showed no signs of tuberculosis. The spleen was enlarged and infiltrated with tubercles. The intestine was generally hyperemic. In the duodenum, the jejunum, and the ileum, at intervals of from 3 to 6 inches, were a number of ulcerations, some flat and broad, others deep, punched out, and undermined, all ulcers running transverse to the axis of the intestine. Scrapings from the ulcers revealed tubercle bacilli. In the caput coli there were two large ulcerated areas, one just above the ileocecal valve, 1½ inches in length and one-half inch wide and the other just at the ileocecal valve, 1 inch long and very irregular in outline. A number of tuberculous ulcers were found in the colon also. Many of the mesenteric glands were enlarged and caseous.

Guinea pigs were inoculated from the spleen and from the mesenteric glands, and all died of tuberculosis.

(7) *Culture D T, human.*—This culture was obtained from the spleen of a guinea pig which had been inoculated with a small fragment of the lung ot a girl 5 years old. The girl was admitted to the Children's Hospital February 28, 1902. The family history was negative. The child was reported to have been ill for approximately three months. On admission to the hospital her temperature ranged from 101° to 107° F. The clinical symptoms warranted a diagnosis of tubercular meningitis associated with pulmonary tuberculosis. The child died on March 10, 1902.

The autopsy was briefly as follows:

Some exudate at the base of the brain; the heart was normal; in the right lung there were a few tubercles. Hemorrhagic areas and tubercles were also found in the upper and lower lobes of the left lung. The liver was softened in places and old adhesions were found on its superior surface. The spleen was soft and exhibited old adhesions. The mesenteric glands were normal, as were the intestines and kidneys. There is nothing in the autopsy record to indicate infection by way of the digestive tract. Smear preparations from one of the lung tubercles showed a few tubercle bacilli.

(8) *Culture E T, human.*—This culture was obtained from the spleen of a guinea pig which was inoculated with a small fragment of a mesenteric gland from a girl 12 years old. The girl had been treated twice in the Children's Hospital for tubercular peritonitis and apparently cured. The first attack occurred during the winter of 1900 and the second in March, 1901. On July 6, 1901, she returned to the hospital suffering from a tuberculous arthritis of the elbow joint. In December, 1901, a complete excision of the joint was made and the child progressed well after the operation. On February 22, 1902, a cold abscess on the back of the neck was opened. On March 8, she began to complain of slight abdominal pain; the temperature rose gradually and the vomiting which occurred was followed rapidly by stupor which deepened into coma and the child died on the morning of March 9. The temperature shortly before death was 108.8° F. There was nothing in the history of this child to indicate the mode of infection.

The autopsy report, which was furnished us by Doctor Mason, is as follows:

Pleuritic adhesions on both sides. The lungs were free from tuberculosis; the heart was small and flabby. The abdominal cavity contained considerable fluid mixed with blood, pus, and intestinal contents. The omentum was much thickened and contained a large number of small tubercles. The omentum and intestines were adherent to the parietal peritoneum. The spleen was large and filled with tubercles; the kidneys were large and soft, but not tuberculous. The liver was very friable and filled with tubercles. The intestines were bound to the peritoneum and the neighboring coils were firmly adherent to each other. There were numerous caseous mesenteric glands; numerous ulcers distributed throughout the ileum. The lower portion of this section of the small intestine was constricted by bands of adhesive tissue and an area of about 7 inches was greatly congested and almost gangrenous. Just above this congested area were two perforations through small ulcers.

Smear preparations made from the mesenteric glands did not show any tubercle bacilli, but the guinea pigs which were inoculated with the same material developed the disease.

(9) *Culture C No. 4, human.*—This culture was obtained from the spleen of a guinea pig which had been inoculated with a small fragment of a peritoneal tubercle from a boy 5 years old. This child was admitted to the Children's Hospital on April 4, 1902. The family history and previous history of the patient as determined at the hospital were as follows: The parents were both alive and healthy, and had lost no children. The only other child was in good health. There was a history of some tuberculosis in the mother's family. The boy when an infant had been reared on condensed milk and until the time of his present illness was said to have been a healthy child. During the summer and fall of 1901 ascites developed and the child was confined to bed for two weeks, the effusion disappearing, but a hard mass remained in the region of the umbilicus. During October, 1901, the patient developed pertussis, and the cough persisted until the time of admission to the hospital. About two weeks before entering the hospital, during coughing, a rupture of the abdominal wall occurred and an intestinal fistula resulted. When admitted to the hospital the child was extremely emaciated, had a severe cough, fever at night, seemed constantly disposed to sleep, and had no appetite. The patient did not improve in the hospital, and died six days after admission.

The autopsy was briefly as follows:

There was a generalized tuberculosis of the thoracic and abdominal viscera involving the lungs, spleen, liver, intestines, and lymph glands. The peritoneum and mesentery contained many tubercles. The mesenteric glands were generally caseous and enlarged. In the lower portion of the ileum was a perforation which connected with a cavity (completely walled off from the peritoneal cavity) which communicated with an opening at the site of the umbilicus. The intestines were so firmly bound down by adhesive tissue that it was exceedingly difficult to trace their course. No ulcers were found. The peritoneal tubercles were examined microscopically but no bacilli found. The guinea pigs which were inoculated developed tuberculosis. It seems probable that the infection in this case as well as in the preceding one, had its origin in the abdominal cavity, but from the rather meager details of the autopsy which are obtainable it is impossible to speak definitely in regard to this matter. On account of the age of the child and its previous good health, the infection most probably took place at some time subsequent to the date when it was weaned from its bottle.

(10) *Cultures Nos. 49 to 60.*—These cultures were of human origin. They had been grown in the laboratory for a number of years on liquid media and still retained the characteristic virulence for guinea pigs.

(11) *Cultures A 101 to A 125.*—These cultures represent different generations of the attenuated culture which has been under cultivation in the Biochemic Division for about ten years. Culture A 125 is the one hundred and fiftieth generation on glycerinized bouillon. This culture was originally received from Doctor Trudeau, who states that it was obtained by himself in 1891 directly from a case of miliary tuberculosis in man. It was afterwards passed through a rabbit and then cultivated on various artificial media. While entirely avirulent for guinea pigs, it has the property of producing in cultures the substance which causes the fever reaction in tuberculous animals, and has for a long time proved very satisfactory for the preparation of tuberculin.

(12) *New York culture, human.*—This culture was obtained December 21, 1901, from a tuberculous lung which was sent to us by Doctor Lartigau, of the College of Physicians and Surgeons in New York. Similar material was also secured from New York on January 6, February 10, and March 3, 1902.

(13) *Sputum, human.*—This material was used for the inoculation and drenching of cattle.

SOURCES OF BOVINE TUBERCULOUS MATERIAL.

(14) *Culture bovine III* (Smith).—This was given us several years ago by Dr. Theobald Smith and since then has been cultivated continuously on glycerinized bouillon.

(15) *Culture C No. 81, bovine.*—This culture was obtained from the spleen of a guinea pig which had been previously inoculated with a fragment of a mediastinal gland from cow No. 81. This animal—cow No. 81—was affected with tuberculosis of spontaneous origin.

Record of cow No. 81: About 5 years old; June 25, 1901, tested with tuberculin; reacted; was removed from the healthy animals and placed in a stable with a number of other cattle which had also reacted to tuberculin; August 26, 1901, had a moist, dry cough, respiration regular and not labored; January 2, 1902, was removed to another stable and confined continuously in a box stall adjoining stalls in which other tuberculous animals were kept. Killed March 13, 1902, and examined postmortem.

Autopsy: Right lung is a solid mass of tubercles excepting a small area at the superior posterior portion of principal lobe. Left lung contains many tuberculous areas, but is not affected to so great an extent as the right one. The tuberculous masses, on section, are found to contain lime salts, and many are broken down. There are also a number of distinct cavities which are partially filled with a gelatinous material. These cavities communicate with the bronchi, which, as well as the trachea, contain a large amount of the above material. The mediastinal glands are enlarged and are converted into masses of tubercles separated from each other by thickened connective tissue. These tubercles, on section, are found to consist of a firm, cheesy material, which contains lime salts. Liver contains several characteristic tuberculous nodules. Spleen apparently normal. Nearly all of the mesenteric glands contain one or more tuberculous foci.

(16) *Bovine tuberculous tissue.*—Material obtained from various cases of spontaneous tuberculosis in cattle.

EXPERIMENTS UPON HOGS.

It will be remembered that Professor Koch[1][a] announced that he had been unable to produce generalized tuberculosis in hogs by subcutaneous inoculations with pure cultures of human origin. In order to determine the correctness of his views we inoculated ten hogs—some with human tuberculous material and some with pure cultures of the human tubercle bacillus—and also one pig with a bovine culture, the latter animal serving as a comparison with those inoculated with human virus. As will be seen from the gross appearance of the various organs obtained from some of these animals, there is little or no difference between the animals inoculated with bovine and human tuberculous material (Pls. VI, VII, VIII, human, and X, XI, XII, bovine). In the case of one pig no disease was produced by inoculation with a human culture. This culture proved to be quite low in virulence for all of the domesticated animals which were exposed to it. The detailed records of the hogs follow:

Record of hog No. 230.—January 29, 1902, tested with tuberculin, without reaction. April 19, 1902, weight 57¼ pounds. Injected subcutaneously inside of right thigh with 1½ c. c. of a suspension of human culture C No. 1 prepared in the following manner: The colonies of tubercle bacilli were scraped from the surface of four dog-serum culture tubes and a watery suspension of them made by adding 18 c. c. of sterile water. A portion of this suspension, which was moderately turbid, was used to inject the animal. September 9, 1902, killed and examined postmortem.

Autopsy: In good condition; no lesions of tuberculosis.

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[a] These figures refer to bibliography on page 98.

Record of hog No. 226.—April 12, 1902, weight before injection, 51 pounds; tested with tuberculin before inoculation without reaction; a piece of thickened tuberculous human intestine, same source as human culture C No. 4, introduced beneath the skin inside of the left thigh; the usual technique employed. September 9, 1902, the animal killed and examined postmortem.

Autopsy: The entire lung was sprinkled with areas of tuberculosis; the left median lobe completely solidified; the bronchial and mediastinal glands greatly enlarged and entirely tuberculous; portal glands similarly affected; a number of necrotic foci in the liver.

Guinea pigs Nos. 2300 and 2301 were each inoculated subcutaneously with a small fragment of a mediastinal gland from this hog and as a result died of a generalized tuberculosis.

Record of hog No. 229.—April 12, 1902, weight 58 pounds; tested with tuberculin before inoculation without reaction; a piece of thickened tuberculous intestine introduced beneath the skin on the inside of the left thigh; the usual technique employed; same material as that used for hog No. 226. September 9, 1902, killed; in good condition.

Autopsy: Sprinkled throughout the lung are numerous minute white points surrounded by a zone of semitransparent material. The mediastinal glands show a number of minute necrotic areas and are slightly enlarged; liver sprinkled with small areas of necrosis, and the portal glands are enlarged and filled with necrotic material; more or less disease of the omentum and serous surface of the intestines, resembling pearl disease; several necrotic areas in the spleen.

The tissue used to inoculate hogs Nos. 226 and 229 was from the same source as that used for obtaining the culture with which hog No. 460 was inoculated.

Record of hog No. 460.—This animal was not tested with tuberculin before inoculation, but was in a perfectly healthy condition at that time. October 13, 1902, injected subcutaneously inside of left thigh with 2 c. c. of human culture C No. 4. This animal showed signs of illness on October 30. The disease advanced quite rapidly, the animal exhibiting a cough, labored respiration, and a poor appetite until November 11, when it was in a dying condition and was killed.

Description of Plate IX.

Sections of organs of hogs inoculated subcutaneously with cultures C No. 4 and E T, human, tuberculosis. Stained with hematoxylin and carbol-fuchsin. Magnified 1,450 diameters.

Fig. 1.—Section of lung of hog No. 457, inoculated with culture E T.

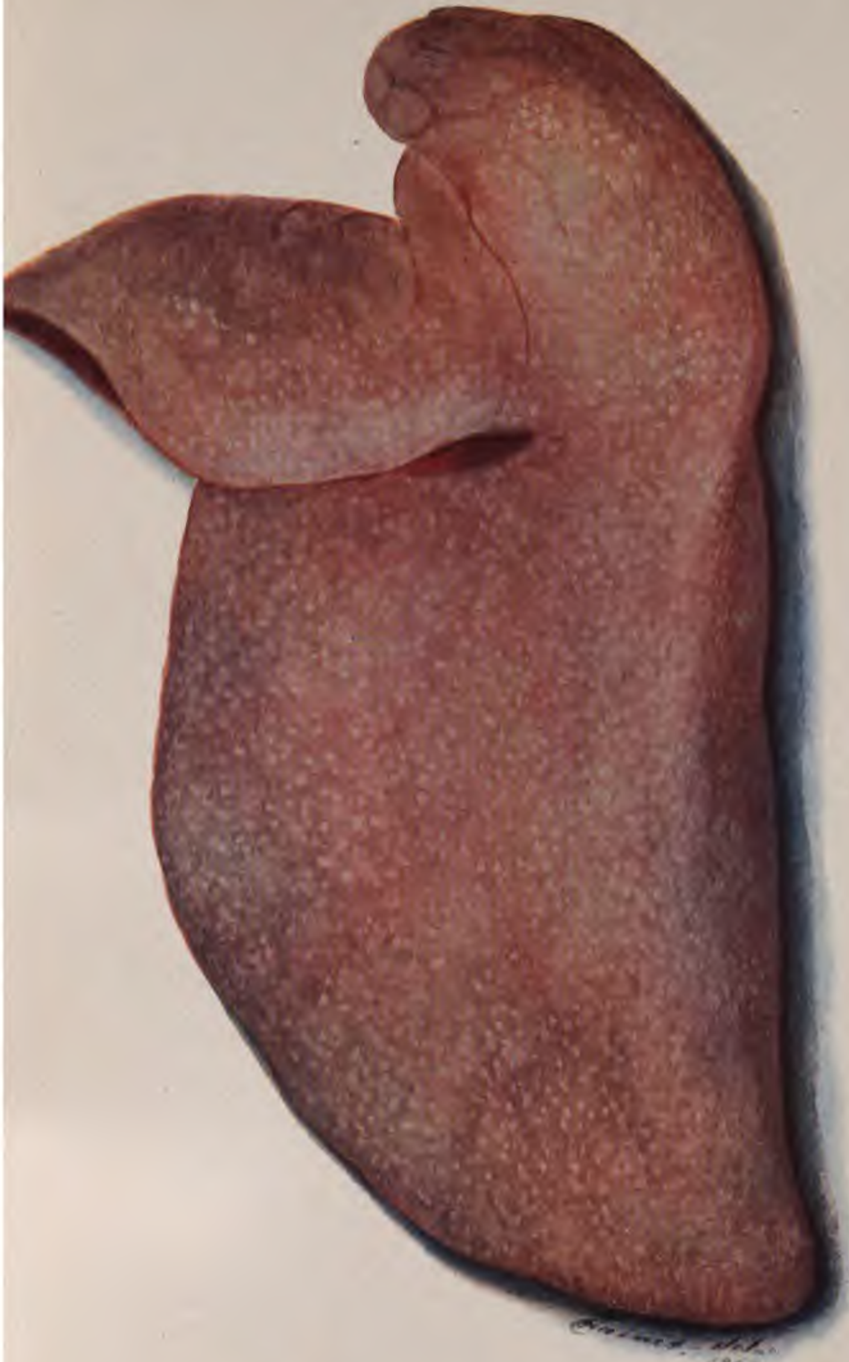
Fig. 2.—Section of spleen of hog No. 457, inoculated with culture E T.

Fig. 3.—Section of liver of hog No. 457, inoculated with culture E T.

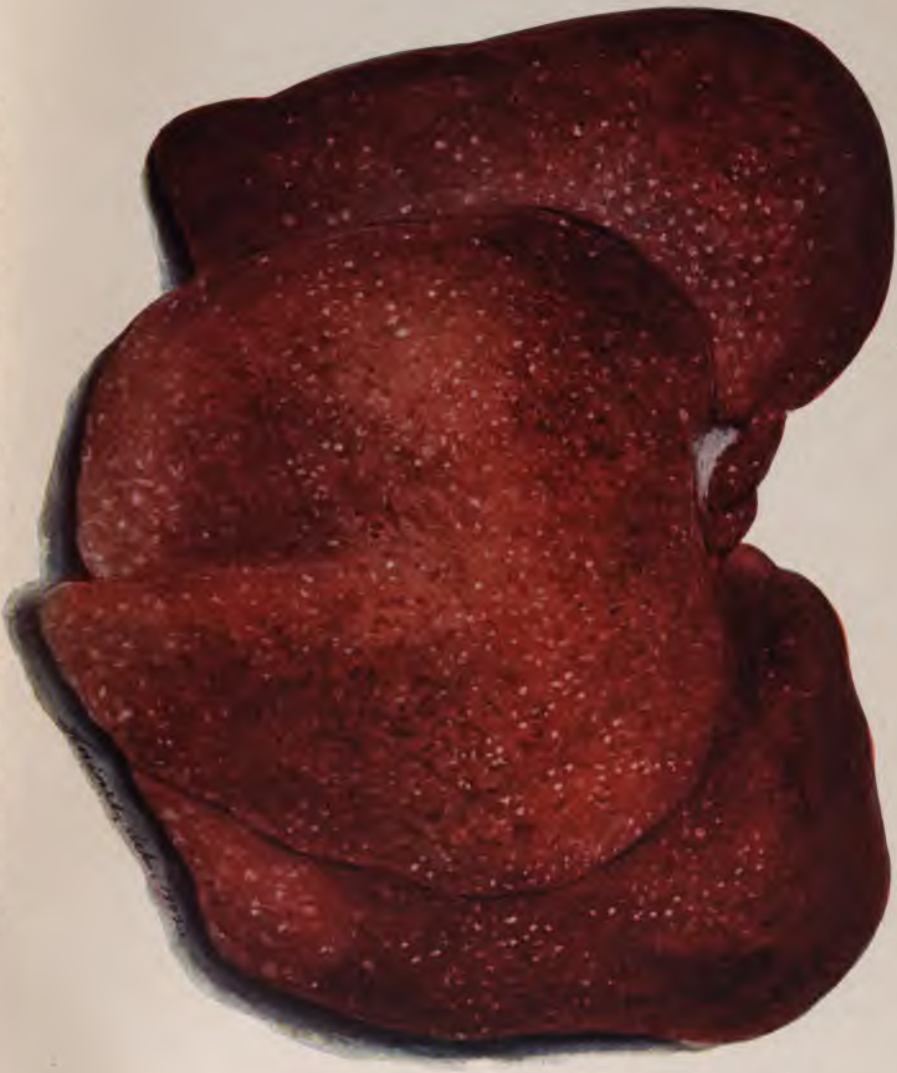
Fig. 4.—Section of lung of hog No. 460, inoculated with culture C No. 4.

Drawing by W. S. D. Haines.

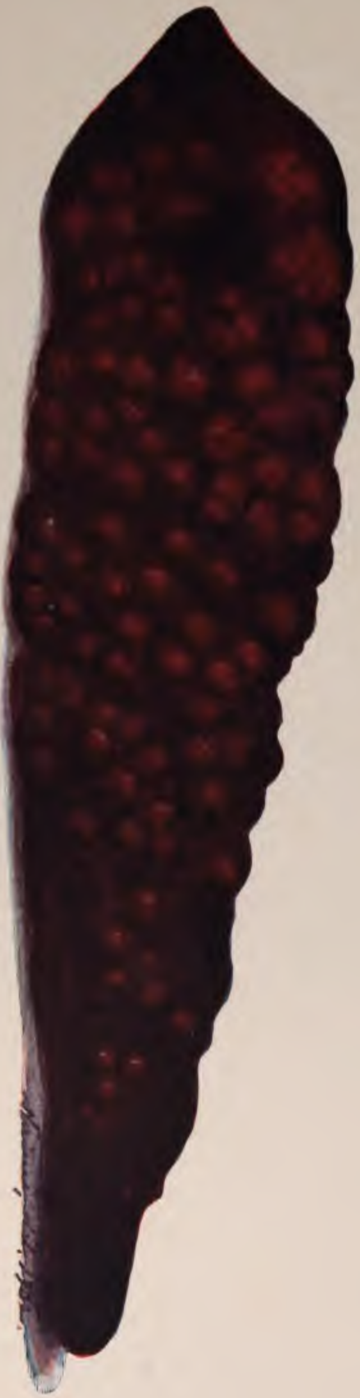
Plate VI.



Lung hog 460. Subcutaneous inoculation with pure culture human tuberculosis No. C 4.



Liver hog 460. Subcutaneous inoculation with pure culture human tuberculosis No. C 4.



Spleen hog 457. Subcutaneous inoculation with pure culture human tuberculosis No. E. T.

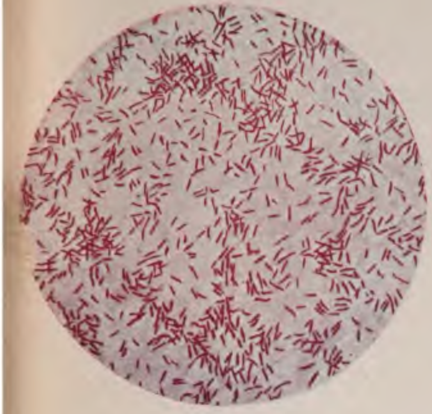


Fig. 1.

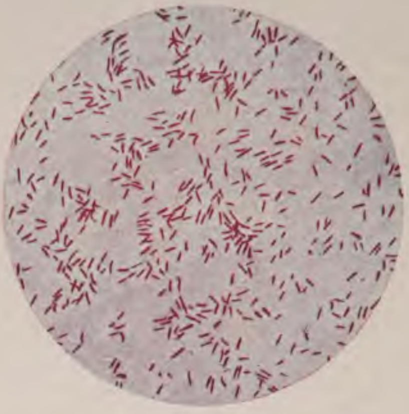


Fig. 2.

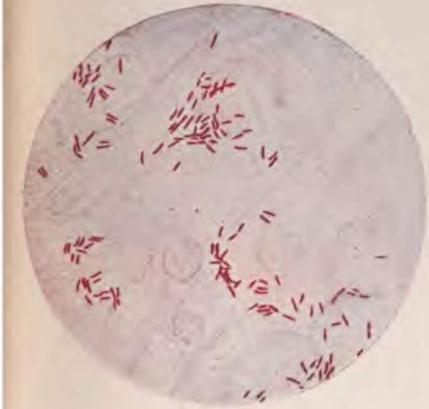


Fig. 3.

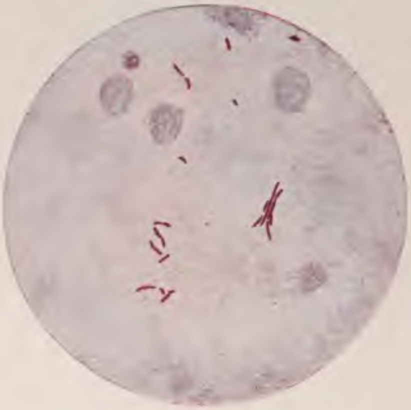


Fig. 4.

Tubercle Bacilli in Sections from hogs. Human Tuberculosis.

Autopsy: Some swelling and slight necrosis of tissue on the inner side of the left thigh was noted. Lymphatic system: (1) Left inguinal glands much enlarged, containing many small yellowish nodules visible on surface of the glands; (2) right inguinal gland and (3) right lumbar gland apparently normal; (4) retroperitoneal glands enlarged; (5) posterior mediastinal glands enlarged, size of pigeon's egg. Spleen very dark red in color; the surface is quite rough and nodular; there is, however, no sign of caseation in the nodules. Liver is paler than normal, and scattered thickly over its surface are grayish white areas, fairly well defined and about the size of a pinhead. Kidneys rather dark, but otherwise normal. Intestines not inflamed, but mucous surface of cecum is covered with a thick white exudate, which is easily peeled off, leaving the intestine beneath in a fairly healthy condition. Lungs have a general pearl-gray color and scattered over their entire surface numerous very minute whitish areas can be distinguished. (See Pls. VI and VII.)

Microscopical examination: Lung—A number of well-defined tubercles with necrotic centers; the tubercles contain a fair number of tubercle bacilli. Liver—A large number of miliary tubercles with necrotic center; occasionally a giant cell can be seen; a few tubercle bacilli are present in some of the tubercles. Spleen—A number of more or less circumscribed areas of necrosis are visible; these areas contain a very few tubercle bacilli. Mediastinal glands—There is considerable necrosis of the cellular tissue and a very few tubercle bacilli are present. Mesenteric gland—A few necrotic areas and a few tubercle bacilli were noted. Left inguinal gland—Large areas of necrosis which contain a few tubercle bacilli. Left lumbar gland—Large areas of necrosis containing very numerous tubercle bacilli. Intestinal exudate—No tubercle bacilli were found.

Record of hog No. 459.—Tested with tuberculin before inoculation without reaction. January 24, 1903, weight 40 pounds; injected subcutaneously inside of left thigh with 2 c. c. of a thin suspension of human culture C No. 4. This animal appeared to be in good condition until June 2, 1903, when it was killed and examined postmortem, lesions of generalized tuberculosis being found.

Record of hog No. 457.—This animal was not tested with tuberculin prior to inoculation, but was in a perfectly healthy condition on October 13, 1902, when it was injected subcutaneously inside of left thigh with 2 c. c. of a thin suspension of human culture E T. This animal gradually lost in condition and died on December 13, 1902.

Autopsy: There was some swelling at seat of inoculation. Lymphatic system—(1) Left inguinal glands very much enlarged and firm; (2) right inguinal glands normal in size and appearance upon section; (3) right lumbar glands apparently normal; (4) retroperitoneal glands enlarged and tuberculous; (5) posterior mediastinal glands very slightly enlarged. Abdominal viscera—(1) Liver about normal size, mottled, and rather light in color; (2) spleen about normal in size, covered with light-red nodules about size of a half pea, some smaller, which are raised above the surface of the organ—a typical tuberculous hog spleen (see Pl. VIII); (3) kidneys congested. Thoracic viscera—(1) Heart, slight pericardial effusion; (2) lungs both gray and almost completely solidified, a number of small grayish points over the surface.

Microscopic examination: The several organs showed as follows: Lung—Large areas are solidified and necrotic; many of the alveoli are filled with cellular débris in which are enormous numbers of tubercle bacilli. Liver—There are large numbers of minute tubercles in the section; these tubercles contain numerous tubercle bacilli. Spleen—A number of large, fairly-well defined tubercles with necrotic centers are to be noted; these tubercles contain great numbers of tubercle bacilli. Mediastinal gland—Contains a moderate number of tubercle bacilli. Left inguinal gland—Tubercle bacilli are present in enormous numbers. Left lumbar gland—Tubercle bacilli are found in enormous numbers.

Record of hog No. 455.—Tested with tuberculin before inoculation, without reaction. January 24, 1903, weight 44 pounds; injected subcutaneously inside of left thigh with 2½ c. c. of a thin suspension of human culture E T. This animal showed no especial signs of illness as a result of the inoculation, but when killed on June 2, 1903, exhibited the lesions of generalized tuberculosis.

Record of hog No. 483.—Tested with tuberculin before inoculation but did not react. January 24, 1903, weight 35½ pounds; injected subcutaneously inside of left thigh with 2 c. c. of a thin suspension of bovine culture C No. 81. March 3, 1903, losing in condition; respiration labored and accelerated; has a tumor at seat of injection about 2 by 2½ inches in size. This hog failed rapidly and died March 9, 1903.

Autopsy: Slight inflammation was found on inside of left thigh; left inguinal gland enlarged and caseous; right inguinal glands normal; left lumbar gland considerably enlarged; mediastinal glands somewhat enlarged. Spleen slightly enlarged and dotted with small round pale areas, some of which are slightly raised above the surface of the organ. Liver has scattered over its surface a fair number of small grayish areas the size of a pinhead or smaller. Lungs were both distended and did not collapse when the thoracic cavity was opened; there was a red hepatization of the cephalic lobes of both lungs; the principal lobes were generally grayish in color and were sprinkled with minute translucent gray areas. (See Pls. X, XI, and XII.)

TABLE III.—*Inoculation of hogs subcutaneously with human and bovine tuberculosis.*

Material used.	Dose.	Number of animal.	Date of inoculation.	Result of inoculation.
	c. c.			
Human culture E T	2	Hog No. 457 [a]	Oct. 13, 1902	Died Dec. 13, 1902.
Do	2.5	Hog No. 455 [b]	Jan. 24, 1903	Remained in fair condition.
Human culture C No. 4	2	Hog No. 460 [c]	Oct. 13, 1902	In dying condition when killed.
Do	2	Hog No. 459 [b]	Jan. 24, 1903	Remained in fair condition.
Bovine culture C No. 81	2	Hog No. 483 [a]	.....do.......	Died March 9, 1903.
Human culture C No. 1	1.5	Hog No. 230 [d]	Apr. 19, 1902	Remained well.
Human intestine (tuberculous).	Small piece.	Hog No. 226 [e]	Apr. 12, 1902	Remained in fair condition.
Do	do	Hog No. 229 [e]	.....do.......	Remained fairly well.

The following footnotes show the condition of the hogs after death:

[a] Generalized tuberculosis.

[b] Killed June 2, 1903. Generalized tuberculosis.

[c] Killed Nov. 11, 1902. Generalized tuberculosis.

[d] Killed Sept. 9, 1902. No tuberculosis.

[e] Killed Sept. 9, 1902. Generalized tuberculosis.

DISCUSSION OF HOG EXPERIMENTS.

From the experiments which have just been described it will be seen that of three cultures of tuberculosis from children, one proved to be practically without virulence for hogs, while the other two induced a generalized tuberculosis which was quite as severe as the disease caused by the bovine bacillus in hog No. 483. The gross lesions brought about in the hogs by the more virulent human cultures and the bovine culture are very well depicted in the accompanying plates (VI to XII).

All the hogs used for these inoculations were in a perfect state of health at the beginning of the experiments.

As a result of these experiments upon hogs, the conclusion is justified that—

1. Certain tubercle bacilli of human origin possess quite as great pathogenic power for hogs as tubercle bacilli of bovine origin.

2. The disease induced in hogs by human cultures, C No. 4 and E T, was distinctly progressive in character, death taking place in two of the animals in twenty-eight and sixty days, respectively.

EXPERIMENTS UPON CATTLE.

Every precaution was taken to avoid the possibility of error in these experiments. In all cases perfectly healthy animals were selected, and no cattle were included in the experiments that had not failed to respond to the tuberculin test. Each animal was kept, after inoculation, in a clean, separate stall, where there was no opportunity for the contraction of disease from other animals. The cattle were inoculated subcutaneously, intraabdominally or intravenously, and some were fed or drenched with tuberculous material. In some instances it was possible to inoculate or drench cattle with human tuberculous tissue and later to inoculate others with pure cultures derived from the same human tissue. By this method we hoped to determine whether the virulence of the organism in question was heightened or lowered during the process of its isolation in pure culture. The dose given the cattle varied somewhat, but was in the main fairly uniform and not excessive, as will be seen by the examination of the records which follow.

INTRAVENOUS INOCULATIONS

Record of heifer calf No. 270.—About one year old; tested with tuberculin without reaction. September 16, 1902, injected with 5 c. c. of a suspension of human tubercle culture F T in right jugular vein. The first symptom of illness was noted on September 25, when the respiration was accelerated. The respiratory disturbance became gradually more marked and the general condition of the animal became worse until about the 17th of October, 1902, at which time signs of improvement were noted. The animal continued to gain rapidly in condition and appetite, and the respiration became normal.

On January 24, 1903, the animal, apparently in perfect health, was inoculated subcutaneously in front of the right shoulder with 5 c. c. of bovine III tubercle culture. As a result of the inoculation with the bovine virus a tumor, 2 by 3 inches in size, developed at the point of inoculation, and the neighboring prescapular gland became considerably enlarged. On May 19, 1903, a soft tumor of considerable size was visible at the point of inoculation; the prescapular gland had returned to its normal size. The enlargement on the side of the neck began to discharge a thick creamy pus on July 27, 1903. On October 24, 1903, a tuberculin test of this animal gave no reaction. The heifer was killed on November 2, 1903, and examined postmortem.

Autopsy: The autopsy showed no lesions of disease. The human culture had evidently not only failed to infect this animal but, on the contrary, apparently had produced an immunity, although such a supposition is open to the rather serious objection that there was no control to prove the pathogenic power of this particular bovine culture for normal cattle.

Record of calf No. 275.—Age, about 9 months; tested with tuberculin previous to inoculation, but did not react. September 16, 1902, injected with 5 c. c. of a suspension of human culture F L into right jugular vein; weight at time of inoculation, 186 pounds. On September 27 the animal was losing in condition and its respiration was accelerated. This calf became gradually weaker until November 3, 1902, when it was killed and examined postmortem.

Autopsy: The pleuræ were considerably thickened and opaque; the lungs showed numerous very minute foci of disease, and the same was true of the liver and kidneys. The mediastinal glands were enlarged, congested, and had the appearance of beginning tuberculosis.

Microscopic examination: Lung—Most of the air spaces in the section are filled with desquamated epithelial cells and leucocytes; there is a slight general increase in connective tissue throughout section; no areas of necrosis were found, but numerous long, well-stained, beaded tubercle bacilli were visible. Kidney—Rather severe cloudy swelling; no distinct tubercles found, but a few long faintly stained tubercle bacilli could be seen. Mediastinal gland—A number of ill-defined areas of coagulation necrosis and a very few long, slender, faintly stained tubercle bacilli.

Although this animal was made quite sick by the intravenous injection of culture F L, the tuberculous lesions found at the autopsy were not progressive in character, and seemed to be hardly greater than might have been expected from the mechanical irritation and the toxic action of the bodies of the injected bacilli. We must consider this case, therefore, as one in which human bacilli failed to produce a true tuberculosis in cattle after intravenous inoculation.

Record of calf No. 272.—About 8 months old; weight, 244 pounds. September 10, 1902, tested with tuberculin, without reaction. September 15, 1902, injected 5 c. c. of human tubercle culture S E No. 3 into right jugular vein. As a result of this inoculation the animal exhibited considerable disturbance of respiration, but did not lose very much in condition.

On December 8, 1902, the calf appeared to be again in a perfect state of health, and having remained well, it was inoculated subcutaneously in front of right shoulder with 5 c. c. of a suspension of bovine tubercle culture III on January 24, 1903. This inoculation of bovine culture produced an extensive local swelling which, in course of time, softened and discharged a thick, creamy pus; the general condition of the animal, however, remained good. On November 6, 1903, this calf was killed and examined postmortem.

Autopsy: The lungs contained a number (50 to 75) of small nodules, which varied in size from 1 to 5 mm. These nodules had a pearl-gray glistening appearance, and in a few instances were surrounded by a zone of congestion. The epicardium showed a little roughening along the groove between the two ventricles. At the seat of the inoculation with the bovine culture the subcutaneous tissues were greatly indurated and sprinkled with several tubercular nodules, which contained a soft, creamy pus. The lymph gland near this point was greatly enlarged, but showed only one nodule of tuberculosis, about 1½ cm. in diameter, which contained thick, creamy pus. Guinea pigs inoculated with fragments of a minute nodule in the lung did not contract tuberculosis.

It is difficult to say positively whether the pulmonary nodules were referable to the intravenous inoculation with human culture S E No. 3 or whether they were caused by the later subcutaneous inoculation with bovine culture III. It seems probable, however, in view of the fact that the bovine virus did not affect the deeper lymph glands, that the nodules in the lungs were caused by the injection of the human tubercle culture. This pulmonary disease was, however, not progressive; the pathological changes were very slight, and apparently did not interfere with the health of the animal, notwithstanding the fact that fourteen months had elapsed between the date of inoculation and the autopsy. On this account we are inclined to consider this inoculation negative in so far as the production of tuberculosis by culture S E No. 3 is concerned.

Record of calf No. 271.—Age, about 8 months; weight, 226½ pounds. September 10, 1902, tested with tuberculin without reaction. September 16, 1902, injected 5 c. c. of human tubercle culture G D into right jugular vein. This animal began to show symptoms of a respiratory disturbance on September 27. This continued for some time without very great effect upon the general health of the calf. On November 4 a rather severe conjunctivitis was noted. This was accompanied by a profuse serous discharge from the eyes. This inflammation did not improve, but, on the contrary, became continually worse. In addition, the animal suffered from a severe diarrhea, which began on November 6 and continued until its death. On November 26 the calf, being in a helpless condition, was killed.

Autopsy: No gross lesions were found, with the exception that the mediastinal glands contained several necrotic foci, the eyeballs were coated with a semiopaque membrane, and the mucosa of the fourth stomach was sprinkled with many elevations. These elevations were from one-eighth to three-sixteenths inch in diameter, and had depressed centers. Liver, spleen, and kidney normal. Lung mottled; some areas of consolidation. Mediastinal glands, rough and nodular. Fourth stomach—The mucous surfaces show some very small white ulcers, and attached to the peritoneal surface are a few nodules the size of a pea.

Microscopic examination: Lung—Numerous slender, beaded tubercle bacilli were found in smear preparations from this organ. In the nodules on peritoneal surface of fourth stomach a moderate number of long, slender, beaded tubercle bacilli were found. In smear preparations from a small ulcer on mucous surface of fourth stomach a few slender, beaded bacilli were found.

In the absence of intestinal lesions of tuberculosis, the severe diarrhea from which this animal suffered can hardly be ascribed to that cause, and as the poor condition of the animal was evidently due directly to the diarrhea, it must be granted that death was not due to the inoculation with the human tubercle bacillus. It is of interest to note, however, that two months after the inoculation macroscopic lesions of tuberculosis, together with tubercle bacilli, were present in the lung and on both the serous and mucous surfaces of the fourth stomach. On the mucous surface of the fourth stomach there was some destruction of tissue.

Record of calf No. 289.—About six months old. October 11, 1902, tested with tuberculin without reaction. October 14, 1902, inoculated intravenously with 5 c. c. of human tubercle culture 12124.

The history of this calf is quite similar to that of calf No. 271. The inoculation with tubercle bacilli produced an accelerated respiration after a time, but the health of the animal did not seem to be seriously impaired until December 20, when an inflammation of the eyes was noted. This affection of the eyes became gradually worse, and was accompanied by a severe diarrhea, the animal losing continually in condition. On February 12, 1903, it was killed. At the autopsy the lungs were found to be sprinkled with a considerable number of small tumors, probably due to the action of tubercle bacilli. This case must be viewed as another failure to produce a progressive tuberculosis in calves by the intravenous injection of human tubercle bacilli, although localized changes were produced in the lungs.

Record of calf No. 273.—About 8 months old; weight 240 pounds. September 10, 1902, tested with tuberculin without reaction. September 15, 1902, injected 5 c. c. of a suspension of human tubercle culture C No. 1 into right jugular vein. The animal exhibited no ill effects as a result of the injection.

On January 24, 1903, it was injected subcutaneously in front of right shoulder with 5 c. c. of a suspension of bovine tubercle culture III. This injection produced quite a large local swelling after a time, and the adjacent prescapular gland became considerably enlarged; the general condition of the animal remained good. On May 18 the local swelling had diminished and the prescapular gland had returned to its normal size. The general condition of the animal remained good, although the tumor at the seat of injection persisted until October 24, 1903, when the calf was tested with tuberculin and a reaction obtained. The animal was killed on November 13, 1903, and examined postmortem.

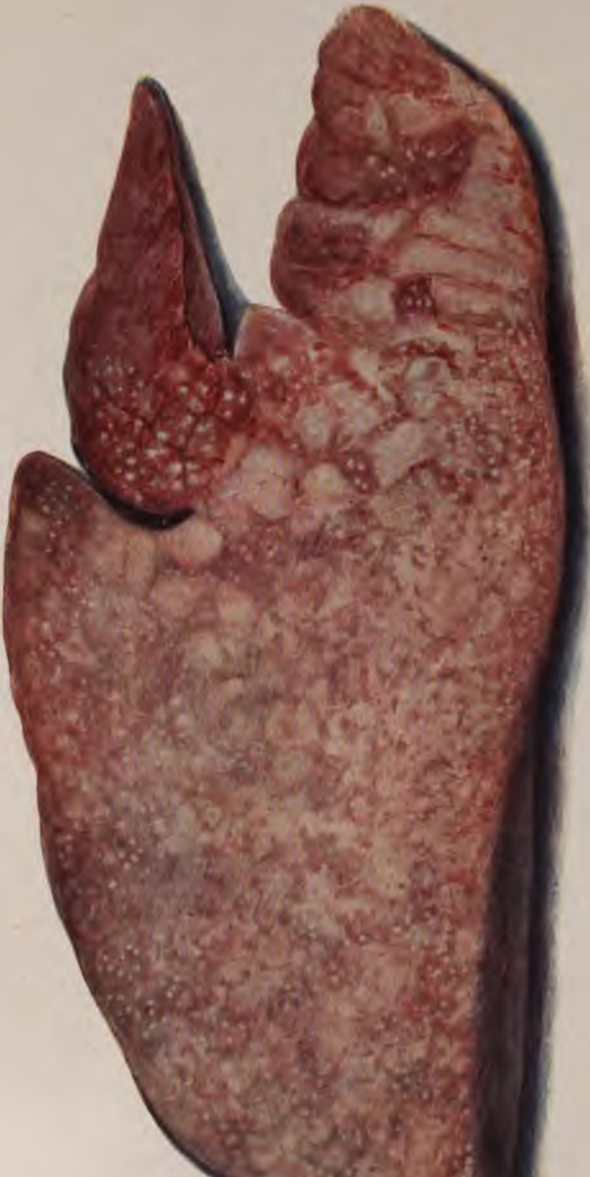
Autopsy: General condition good. A tumor about 2 inches long and 1 inch thick, consisting of a thin wall inclosing a mass of thick, soft pus was found at the seat of injection on the right side. The gland adjacent to the injection tumor is greatly enlarged and contains several tubercles 5 mm. in diameter. Other superficial glands are normal. Lung—Mediastinal glands are considerably enlarged, but free from disease; sprinkled over the pleura of the lung are numerous tubercles from 1 mm. to 5 cm. in diameter; a few small tubercles in the lung tissue proper; the number of tubercles on the costal pleura and on both sides of the diaphragm. Liver—Several tubercular masses on the surface of the liver from 1 to 3 cm. in diameter. Other organs normal.

Owing to the absence of any symptoms of illness following the inoculation with the human culture, the lesions found at the autopsy must be attributed, at least in great part, to the action of the bovine bacilli. This calf did not, therefore, acquire immunity from the bovine bacillus as a result of the previous intravenous injection with the human culture.

Record of calf No. 264.—Age about 5 months. Tested with tuberculin, but did not react. August 9, 1902, injected 5½ c. c. of a suspension of human tubercle culture E T into jugular vein. No symptoms of illness were noted until August 19, when the respiration was accelerated and the temperature high. From this date until the day of its death the animal became rapidly worse. There was loss of appetite, listlessness, emaciation, and an uncertain gait. The respiration was short and jerky, with an occasional cough. On August 29, 1902, twenty days after injection, the calf died and was examined postmortem.

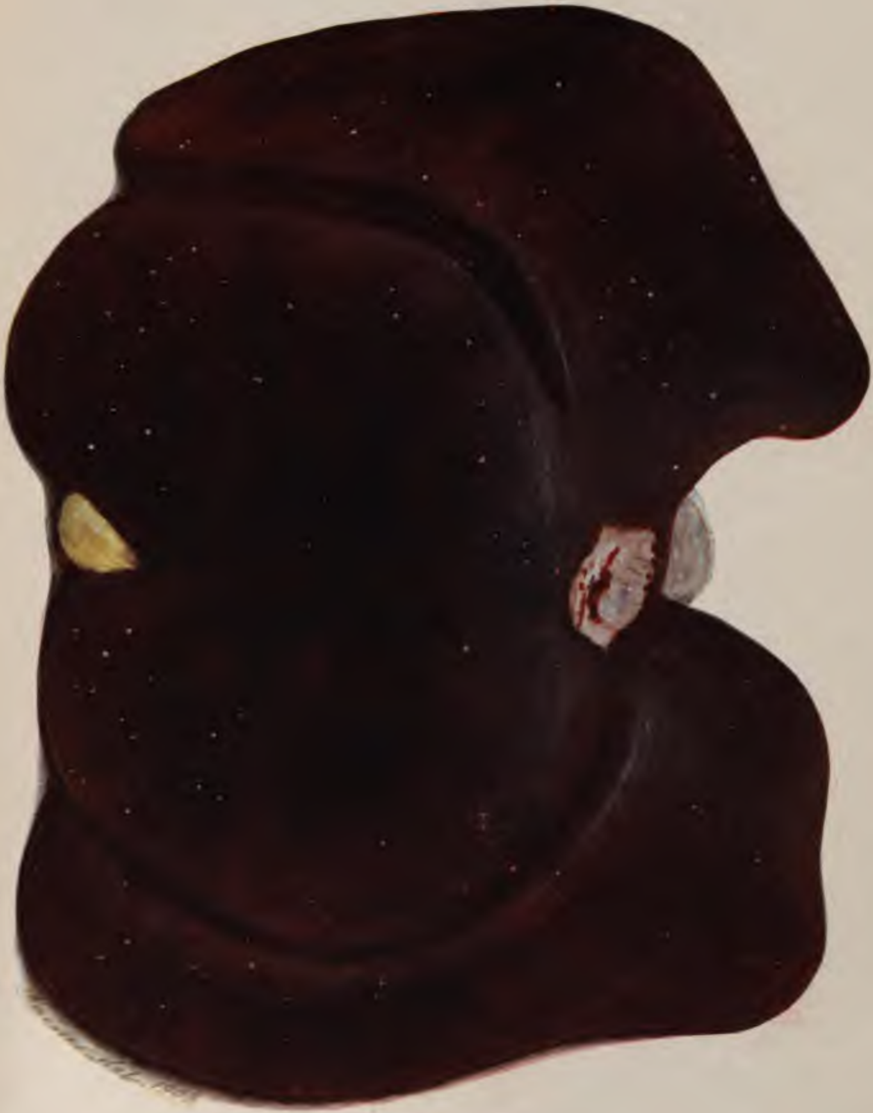
Autopsy: Animal greatly emaciated. Mediastinal glands greatly enlarged, edematous, and congested. Lung intensely congested; the anterior lobes are in a state of collapse, and show numerous hemorrhages under the pleura; sprinkled over the surface are numerous minute necrotic areas; on section the lung has a finely granular appearance, apparently a miliary tuberculosis of the entire organ; bronchial tubes show some slight congestion, and the smaller tubes contain a small amount of viscid mucus. Liver—Greatly swollen, edges rounded; the centers of the lobules appear as pale, yellowish gray points of irregular outline. Portal lymph glands pale but very edematous. Spleen—Enlarged and softened; trabeculæ and Malpighian corpuscles distinct. Kidneys—Redder than usual, and show a sprinkling of white areas, few in number. Mesenteric glands edematous and congested. The glands at the brim of pelvis and just inside of the anterior portion of thorax are apparently normal. Throat glands edematous.

Microscopic examination: Lung—The lung tissue examined in section was infiltrated with cells, and there were a number of miliary tubercles scattered throughout it, all of which contained numerous tubercle bacilli. Liver—No distinct tubercle formation was observed, but a number of well-stained tubercle bacilli were seen in various portions of the section, usually in small clumps. The liver showed rather extensive fatty changes. Kidneys—Marked parenchymatous degeneration; no tubercle formation, though a few tubercle

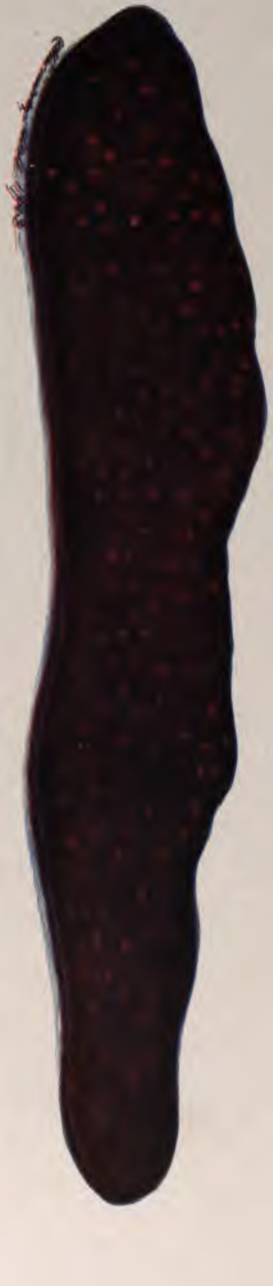


Lung hog 483. Subcutaneous inoculation with pure culture bovine tuberculosis No. 81.

Plate XI.

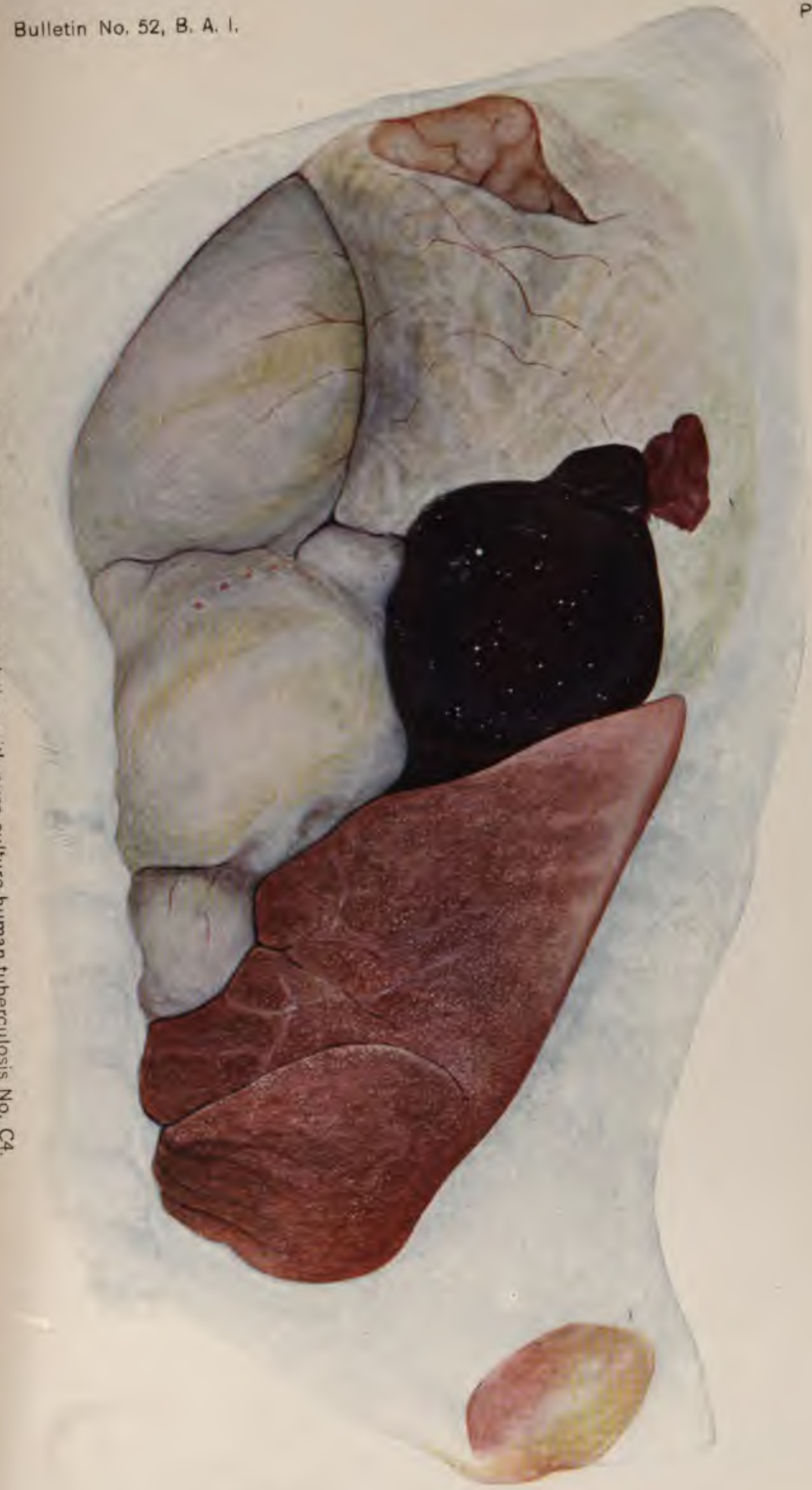


Liver hog 483, subcutaneous inoculation with pure culture bovine tuberculosis No. 81.



Spleen hog 483. Subcutaneous inoculation with pure culture bovine tuberculosis No. 81.

Plate XIII.



Calf 286. Subcutaneous inoculation with pure culture human tuberculosis No. C4.

bacilli were found in smears. Spleen—No sharply defined tubercles were seen, although there were some rather large areas of coagulation necrosis in which were found some giant cells and a large number of tubercle bacilli. Mediastinal gland; a very large number of well-stained tubercle bacilli were seen throughout the section; in some places there was a beginning necrosis of the cellular tissue and here the tubercle bacilli were especially abundant. Mesenteric gland—The portions seen in section were apparently normal, although a very few tubercle bacilli were found in smears from this gland. A guinea pig inoculated with a bit of lung tissue from calf No. 264 died of generalized tuberculosis.

There can be no doubt as to the result of this experiment. The human culture used for intravenous injection produced a severe generalized tuberculosis and was evidently directly responsible for the death of the calf. It is instructive to compare this autopsy with that of calf No. 260, inoculated with bovine III culture.

Record of calf No. 265.—Age, about 5 months. Tested with tuberculin before inoculation without reaction. August 9, 1902, injected 5½ c. c. of a suspension of human tubercle culture D T into right jugular vein. Began to lose in condition on August 22, 1902, but did not seem to be seriously ill until August 30, when the respiration had become very much accelerated and the animal appeared to be failing rapidly. The respiration became more rapid and labored and the emaciation and weakness gradually more marked. The calf was found dead September 8, 1902, thirty days after injection.

Autopsy: Lung very much congested and edematous; on section showed evidences of extensive broncho-pneumonia; other organs in very much the same condition as described for calf No. 264.

Microscopic examination: Lung—Large areas are solidified; a few tubercle bacilli were found in smears. Liver has undergone extensive degenerative changes; no tubercle bacilli could be found, but great numbers of a large bacillus which did not stain by Gabbett's method were found in the blood vessels. Spleen—No tubercle bacilli could be found, but there were enormous numbers of bacilli of the kind found in liver. Kidney—No tubercle bacilli could be found; the sections showed extensive cloudy swelling and the blood vessels were filled with the same large organism which was found in liver and spleen. Mediastinal gland—Smears showed fairly numerous tubercle bacilli and in the section many of the large bacilli previously mentioned were seen. A guinea pig inoculated subcutaneously with a bit of lung from calf No. 265 died of generalized tuberculosis.

Although at the autopsy the lesions gave every indication that the animal died of a severe generalized tuberculosis quite similar to the disease to which calf No. 264 succumbed, we are led to doubt this as a result of the microscopic examination. No tubercle bacilli could be found in any of the organs with the exception of the lungs and mediastinal gland. In addition, the kidneys, spleen, and liver contained enormous numbers of an unidentified bacillus which was not acid fast. Under these circumstances the probability of a secondary infection seems very great, and the tuberculosis injection can not be considered as having produced, unaided, the lesions found at the autopsy. Unfortunately, this secondary infection was not suspected until the sections were examined, and we were therefore unable to study cultures of the organism associated with it.

Record of calf No. 274.—About 7 months old; weight, 230 pounds. Tested with tuberculin prior to inoculation and did not react. On September 15, 1902, 5 c. c. of a suspension of human tubercle culture C No. 4 was injected into right jugular vein. The calf remained well until September 24, 1902, when its respiration was accelerated. Beginning on this date it lost rapidly in condition, became emaciated, lost appetite, and respiration became labored. On October 2, 1902, the animal died and was examined postmortem.

Autopsy: Animal greatly emaciated; the pulmonary pleura was roughened and some portions presented small circular elevations the size of a pinhead. The lung tissue had a granular appearance on section; the dependent portions of the anterior lobes were considerably congested. Liver and kidneys congested. Some of the mediastinal glands congested.

Microscopic examination: Lung—Sections show a great unmber of miliary tubercles, all of which contain large numbers of tubercle bacilli. Liver—Many of the liver cells are undergoing a fatty degeneration; they are granular, and many have lost their nuclei; no distinct tubercles were found, although a number of clumps of tubercle bacilli, as well as scattered separate tubercle bacilli, well stained, were distributed throughout the organ. Spleen—Section shows a number of irregular areas of necrosis which contain large well-stained tubercle bacilli. Mediastinal gland—Some necrotic foci, which contain many large tubercle bacilli. Two guinea pigs inoculated, respectively, with bits of lung and spleen died of generalized tuberculosis.

From the foregoing record it is apparent that calf No. 274 died of a generalized tuberculosis which was brought about by the intravenous injection of human culture C No. 4. The result in this case may also be instructively compared with the results obtained in calves Nos. 260 and 264.

Record of calf No. 260.—Age, 5 months. Tested with tuberculin without reaction. July 19, 1902, 20 c. c. of a suspension in beef broth of bovine culture III was injected into the jugular vein. On July 30 the animal was spiritless, the appetite poor, and respiration accelerated. Beginning on this date the calf lost rapidly in condition, the respiratory disturbance became more marked, and the appetite was lost completely. The animal was found dead on the morning of August 6, 1902.

Autopsy: Postmortem decomposition had progressed so far that it was difficult to make a satisfactory examination. Lungs almost completely solidified; on section they had a granular appearance. Liver had undergone considerable postmortem changes, but did not appear to be diseased. Spleen, kidneys, and lymph glands, with the exception of the mediastinal, appeared to be free from disease.

Microscopic examination: Lung—Smear preparations from this organ showed very many tubercle bacilli. The mediastinal gland also exhibited in smear preparations a considerable number of tubercle bacilli. Sections from the kindey showed neither tubercle formation nor tubercle bacilli, but considerable parenchymatous nephritis was present.

TABLE IV.—*Intravenous inoculations of calves.*

Material used.	Dose.	Number of animal.	Age of animal.	Date of inoculation.	Result of inoculation.
	c. c.				
Human culture F T	5	Calf No. 270[a]	1 year	Sept. 16, 1902	Recovered.
Human culture F L	5	Calf No. 275[b]	9 mos	do	Killed Nov. 3, 1902.
Human culture S E No. 3	5	Calf No. 272[c]	8 mos	Sept. 15, 1902	Recovered.
Human culture G D	5	Calf No. 271[d]	8 mos	Sept. 16, 1902	In moribund condition Nov. 26, 1902; killed.
Human culture 12124	5	Calf No. 289[e]	6 mos	Oct. 14, 1902	Killed Feb. 12, 1903.
Human culture C No. 1	5	Calf No. 273[f]	8 mos	Sept. 15, 1902	Recovered.
Human culture E T	5½	Calf No. 264[g]	5 mos	Aug. 9, 1902	Died Aug. 29, 1902.
Human culture D T	5½	Calf No. 265[h]	5 mos	do	Died Sept. 8, 1902.
Human culture C No. 4	5	Calf No. 274[i]	7 mos	Sept. 15, 1902	Died Oct. 2, 1902.
Bovine culture III	20	Calf No. 260[k]	5 mos	July 19, 1902	Died Aug. 6, 1902.

The following footnotes show the condition of the calves after death:

[a] After recovery from inoculation with human virus received bovine culture subcutaneously. No lesions at autopsy.

[b] Lesions found at autopsy were apparently not progressive.

[c] After recovery received subcutaneous inoculation of bovine culture. At autopsy lesions found in lung, but not severe.

[d] Lesions of tuberculosis not sufficient to account for condition at time animal was killed.

[e] Necrotic areas in lungs. Tuberculous lesions not sufficient to account for poor condition when killed.

[f] After recovery received subcutaneous inoculation of bovine culture. When killed later, found tuberculous lesions; probably due to bovine culture.

[g] Postmortem showed a severe generalized tuberculosis.

[h] Lesions of generalized tuberculosis. The microscope disclosed a contaminating organism, and fatal result may have been partly due to that cause.

[i] The postmortem examination disclosed a generalized tuberculosis.

[k] Tuberculosis involving lungs and some lymph glands.

SUBCUTANEOUS INJECTIONS.

Record of calf No. 250.—About one year old; tested with tuberculin without reaction. April 12, 1902, a piece of tuberculous human lung tissue having a volume of one-half cubic inch was introduced beneath the skin, back of left shoulder of this calf; a piece of thickened tuberculous intestine having a volume of about one-half cubic inch was introduced in like manner back of right shoulder. The diseased lung and intestine were derived from the same case of tuberculosis from which culture C No. 4 was obtained. On May 14, 1902, there was no lesion on the right side at seat of inoculation, but on the left there was a tumor about 3 by 3 inches in area. It had a soft center and had been discharging. The general condition of the animal was poor. As the animal did not improve, it was tested with tuberculin on June 19, 1902, and gave a good reaction. On September 10, 1902, it again gave a partial reaction to tuberculin. On October 1, 1902, the calf was killed and examined postmortem.

Autopsy: At seat of inoculation on left side there was a group of small abscesses in the skin; at seat of inoculation on right side a small subcutaneous tumor with walls of connective tissue streaked with hemorrhagic lines. The contents of the tumor consisted of broken-down necrotic material. The superficial glands in front and back of shoulders and in the flank contained numerous necrotic foci; on the pleuræ of the lung and chest wall were numerous pale-red excrescences, particularly plentiful on the right side, in the dorsal region, and on the posterior border of the principal lobe. Similar growths were attached to the diaphragm; these growths extended about one-fourth to one-third of an inch above the surface of the diaphragm and appeared as isolated, almost circular, elevations about one-half inch in diameter, or as patches made up of numerous similar growths which had coalesced and which varied from one to four inches in diameter. No lesions were found in the lung tissue or in the mediastinal glands.

Microscopic examination: Flank gland—Caseous material from this gland, in which was a considerable amount of lime salts, contained large numbers of tubercle bacilli. Shoulder gland—This gland, which had a caseous center containing a considerable amount of lime salts, also exhibited many tubercle bacilli in cover-glass preparations. Pulmonary excrescences—The section showed a large amount of newly formed connective tissue, many lymphoid cells, and many small blood vessels; there was no evidence of necrotic change; a not inconsiderable number of tubercle bacilli were found.

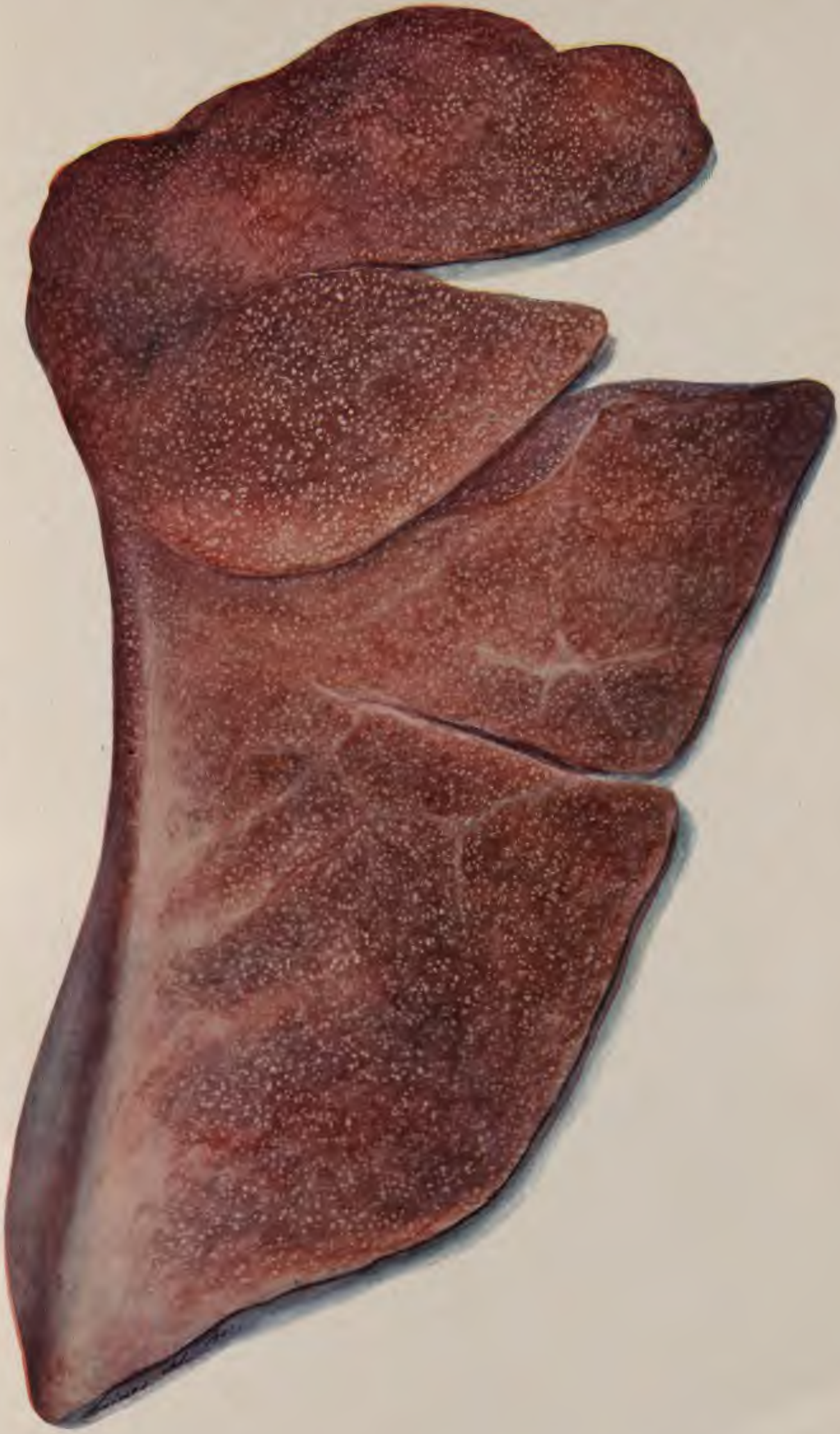
DESCRIPTION OF PLATE XVI.

Sections showing distribution of tubercle bacilli in organs of calf 286, inoculated subcutaneously with C No. 4, human culture. Stained with hematoxylin and carbol-fuchsin. Magnified 1,450 diameters.

Fig. 1.—Section of lung.

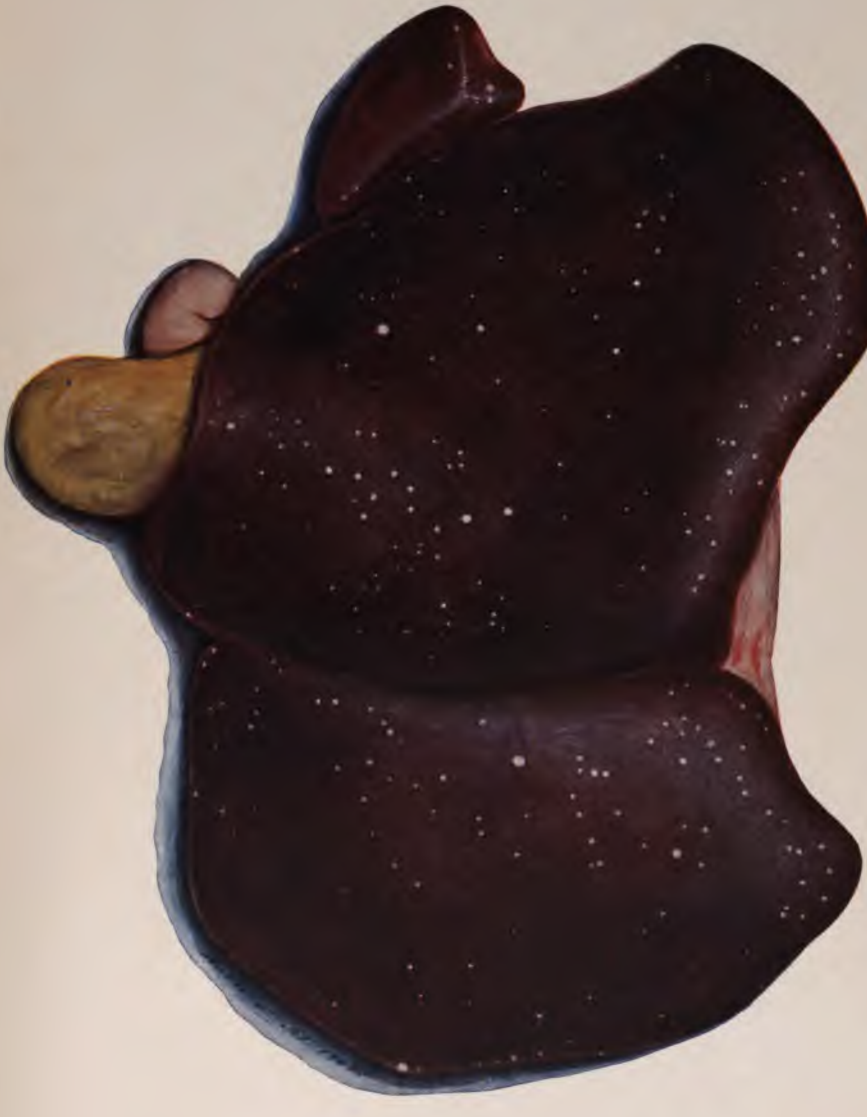
Fig. 2.—Section of spleen.

Drawing by W. S. D. Haines.



Lung Calf 286. Subcutaneous inoculation with pure culture human tuberculosis No. C 4.

Plate XV.



Diaphragmatic excrescence—The appearance was very similar to that of the pulmonary excrescences, except that the process was not so far advanced, there being a less amount of fibrous tissue and more of the cellular elements; a few giant cells and a very few tubercle bacilli could be seen in different parts of the sections. Guinea pigs inoculated, respectively, with bits of the flank gland, pulmonary excrescence, and diaphragmatic excrescence all died of generalized tuberculosis.

By this inoculation we have produced a tuberculosis which though not fatal, was distinctly progressive in character and we therefore consider this case as one in which we have successfully infected a calf with human tuberculosis. Comparison between the record of this calf and the records of calves Nos. 286 and 274 shows the difference between the result of inoculation with tissues on the one hand and pure cultures on the other.

Record of calf No. 286.—About 6 months old. Tested with tuberculin before inoculation; did not react. On October 13, 1902, this animal was injected subcutaneously on the right side of neck, directly in front of shoulder, with 5 c. c. of a suspension of human tubercle culture C No. 4. On October 23, 1902, this calf had a swelling about 3 by 3 inches in area at seat of injection, and the adjacent prescapular gland was much enlarged. On October 27, 1902, the swelling persisted and the animal was evidently losing condition. Appetite became very poor and the weakness gradually more pronounced. There seemed to be no disturbance of respiration during the early part of its illness, but on November 14, 1902, the breathing was labored. On this date the calf was unable stand alone and in a dying condition, and was killed and examined postmortem.

Autopsy: The animal was extremely emaciated; at seat of injection the skin was indurated over an area about 4 inches square; under this induration the gland in front of shoulder was 4 by 3 inches in size. Axillary gland on side of injection was normal; gland on same side was normal. Lungs—The entire lungs the exception of the dorsal portions of the principal lobes intensely reddened and sprinkled throughout with minute cles. Liver normal in color, and sprinkled with numerous necrotic areas, apparently tuberculous in character, varying from mere points to one-eighth inch in diameter. Spleen ged and filled with small, round, firm, white nodules, the size shot, which are easily picked out of organ. Sprinkled entum were a number of small pearl-gray nodules with ters, probably tubercles. Glandular system—Prescap- immediately beneath point of injection) greatly enlarged; not caseous; entire gland quite firm. Pharyngeal glands considerably enlarged; a number of small, firm, yellowish nodules in the body of the gland. Mediastinal glands considerably enlarged; the surface was rough; there were no caseous areas. Pubic glands about normal in size, but contained one or two small areas that looked suspiciously like tuberculous foci. Mesenteric glands apparently slightly enlarged. Shoulder gland normal in size and appearance. Flank gland normal. (See Pls. XIII, XIV, XV, and XVI.)

Microscopic examination: Lung—A number of well-defined miliary tubercles were visible in the sections. The central portion of most of the tubercles had undergone a coagulation necrosis and they were in some instances homogeneous and structureless and in others consisted of a mass of nuclear fragments which stained with hematoxylin; all of the tubercles contained a considerable number of rather large tubercle bacilli. Liver—Several large tubercles were found in the sections; the central portions of them were necrotic and they contained a number of well-stained tubercle bacilli. Spleen—This organ contained a number of rather large, well-defined tubercles, most of which had necrotic centers and contained a number of tubercle bacilli, well stained, rather long, many of them beaded. Kidney—A smear from one of the tubercles showed quite numerous tubercle bacilli. Prescapular gland—Large areas of coagulation necrosis, not sharply defined; many well-stained tubercle bacilli were scattered throughout the tissue, more numerous in some places than others. Gland just inside thorax—Some large areas of necrosis and many well-stained tubercle bacilli were found. Pharyngeal gland—A few large, poorly defined areas which were undergoing degenerative changes; a considerable number of well-stained tubercle bacilli could be seen in the affected portions of the tissue. Shoulder gland—No tuberculosis. Flank gland—No tuberculosis. Mediastinal gland—Many tubercle bacilli found. Intestines—No tuberculosis. Suprarenal body—No tuberculosis. Pubic gland—Tubercle bacilli fairly numerous.

From the record of this experiment it will be seen that we have in this instance a generalized tuberculosis in a calf produced by subcutaneous injection of a culture of human tuberculosis. This record should be carefully compared with that of calf No. 284, which was injected subcutaneously with a culture of bovine origin.

Record of heifer calf No. 288.—October 2, 1902; a small animal in fairly good condition, about 6 months old. October 11, 1902, tested with tuberculin without reaction. Injected October 13 subcutaneously on the right side of neck directly in front of shoulder with 5 c. c. of a suspension of human tubercle culture E T. This animal developed an extensive swelling 4 by 5 inches in diameter at the seat of injection. There was, however, very little evidence

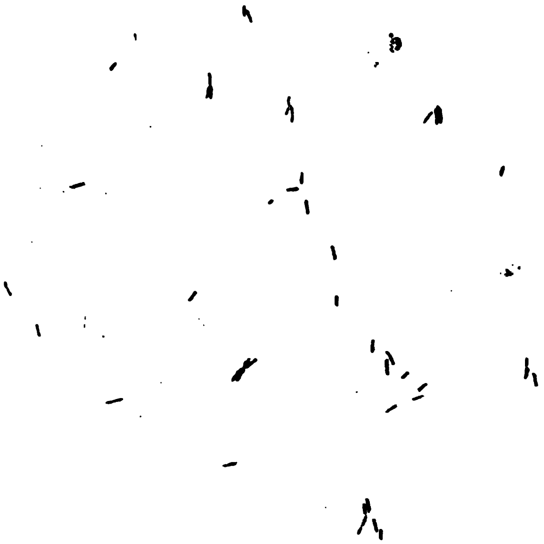


Fig. 1.

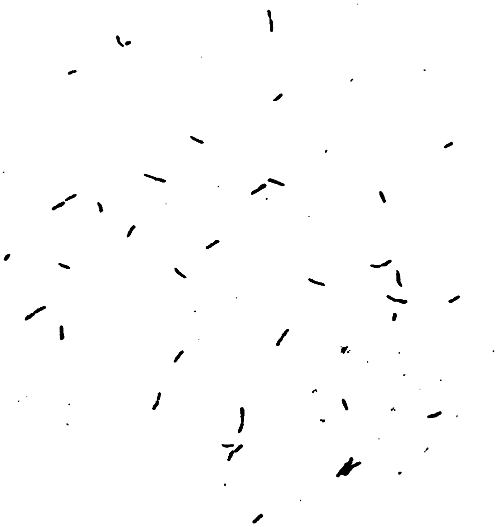


Fig. 2.

Tubercle bacilli in sections from Calf 286. Human tuberculosis.

Record of calf No. 285.—October, 1902, red-and-brown heifer about 13 months old, tested with tuberculin without reaction. January 24, 1903, injected subcutaneously in front of right shoulder with 5 c. c. of a suspension of human tubercle culture E T. February 3, 3, 1903, had a lesion at seat of injection which was continuous with the prescapular gland. The latter was about 2 by 5 by 3 inches in size. The general condition of the animal was fairly good. February 13, 1903, prescapular gland and tumor at seat of injection had coalesced, forming a hard enlargement about 4 by 9 by 3 inches in size; general condition poor. February 26, 1903, tumor at seat of injection and nearest prescapular gland have a combined volume of about 6 by 10 by 3½ inches; this enlargement is very hard; general condition is poor; respiration seems to be normal. April 28, 1903, killed and examined postmortem.

Autopsy: Animal in fairly good condition, not fat; at seat of injection in front of right shoulder the lymph gland was about 6 by 5 by 4 inches in size and very firm; a number of small calcareous nodules in the mediastinal glands; the lungs and spleen were dotted here and there with small tubercles.

This animal was inoculated as a control on calf No. 288, and, as will be seen from the record, developed a generalized tuberculosis, which was not so severe, however, as that produced in calf No. 288. Calf No. 285 was about 7 months older than calf No. 288.

Record of calf No. 287.—About 6 months old. October 11, 1902, tested with tuberculin without reaction. October 13, 1902, injected subcutaneously on right side of neck directly in front of shoulder with 5 c. c. of a suspension of human tubercle culture D T. On October 23, 1902, this animal presented a large swelling at the point of injection, and the prescapular gland which was directly beneath this point was enlarged. There were practically no symptoms other than the local lesions as a result of the injection. On December 19, 1902, this calf was killed and examined postmortem.

Autopsy: A large tumor 5 by 3 inches at seat of injection; this tumor was hard, the central portion was necrotic but not softened. Prescapular gland about 3 by 1½ inches; the cortical portion contained tuberculous foci with considerable deposits of lime salts. Gland just inside thorax; about the size of a walnut; a large portion

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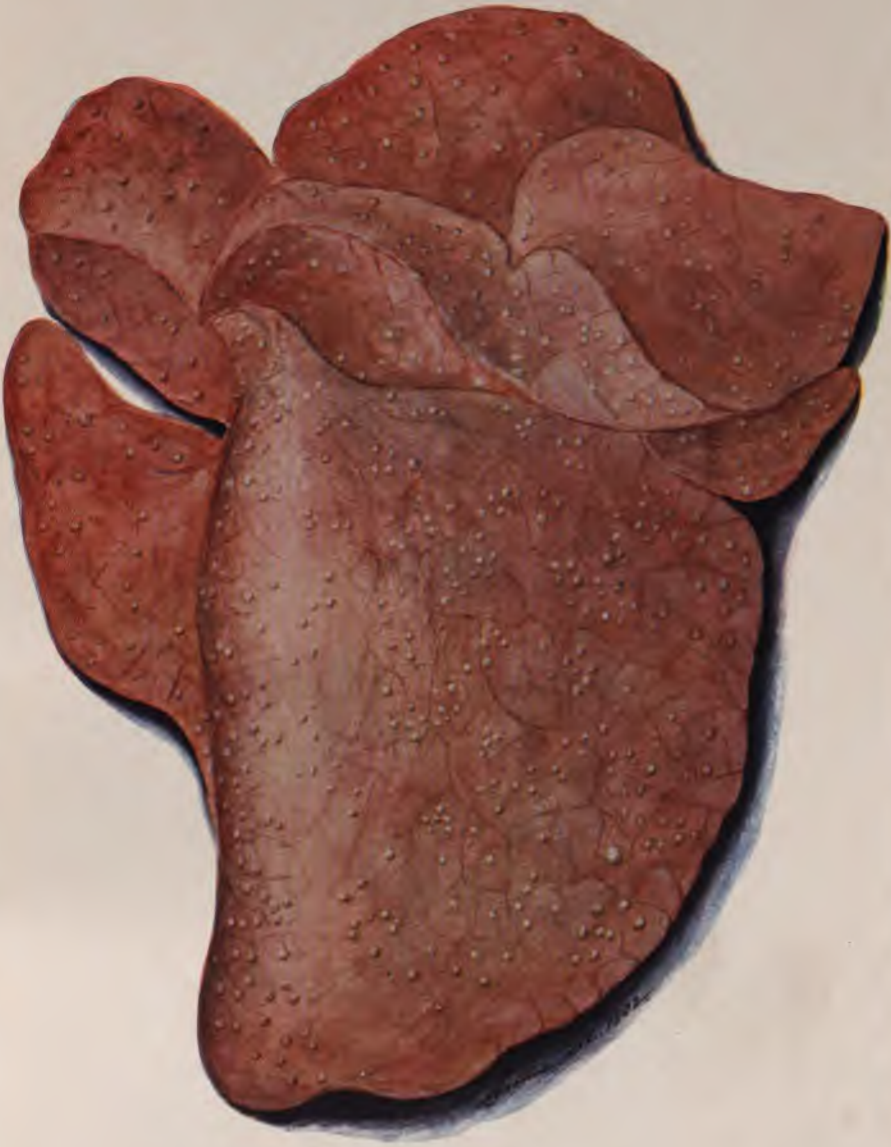
DESCRIPTION OF PLATE XIX.

Reproduction of a smear and a section from tissues of calf No. 288 inoculated subcutaneously with human culture E T, indicating the distribution of bacilli. Stained with hematoxylin and carbol-fuchsin. Magnified 1,450 diameters.

Fig. 1.—Smear made from lung.

Fig. 2.—Section from a mesenteric gland.

Drawing by W. S. D. Haines.



Calf 288. Subcutaneous inoculation with pure culture human tuberculosis No. E. T.

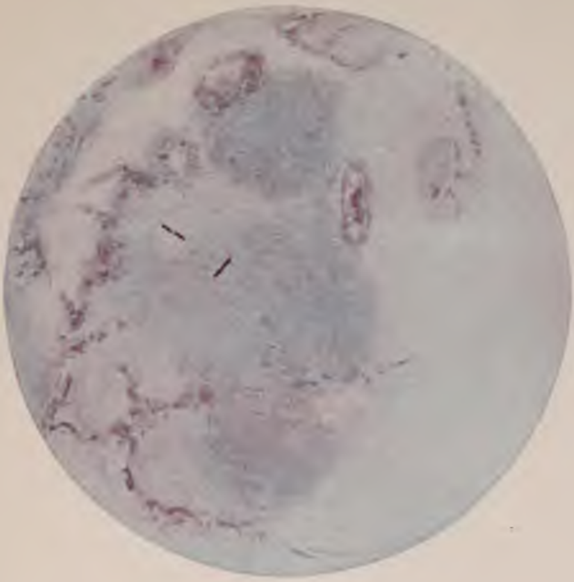


Fig. 1.

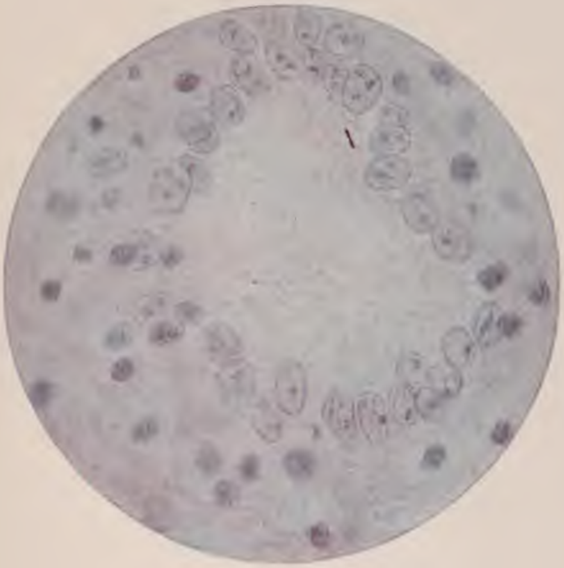


Fig. 2.

Tubercle bacilli from Calf 288. Human tuberculosis No. E. T.

of the gland was necrotic and contained abundant lime salts. This animal was otherwise normal.

Microscopic examination: At point of injection numerous rather large, well-stained tubercle bacilli were found. Smear preparations from prescapular gland contained a few well-stained tubercle bacilli. Gland just inside thorax contained a very few tubercle bacilli.

It is evident that culture D T is distinctly lower in pathogenic power for cattle than either culture E T or C No. 4. It appeared, however, to be possessed of nearly if not quite as great pathogenic power as the rather feeble bovine III culture, and after subcutaneous injection succeeded in invading the lymph glands adjacent to the seat of injection.

Record of calf No. 221.—About 18 months old; gave negative result to tuberculin test. Injected subcutaneously in front of right shoulder with 6½ c. c. of a dilute suspension of human culture G D September 23, 1902. The calf showed no signs of illness as a result of the inoculation. Was tested with tuberculin in June, 1903, and gave no reaction. In November, 1903, the animal being in excellent physical condition, was exposed to natural infection with bovine tuberculosis by being placed in the stall with tuberculous cattle. No symptoms of illness resulted, although several other animals placed under similar conditions contracted tuberculosis.

The calf was killed August 17, 1904, and examined postmortem. No lesions of any kind were found. This experiment was therefore entirely negative in so far as the injection of the calf with human tuberculosis is concerned. The calf evidently possessed considerable resisting power to natural infection. The probability of this immunity having been conferred by the injection of culture G D will be discussed in Part III of this bulletin.

Record of calf No. 290.—About 6 months old; tested with tuberculin without reaction. Injected subcutaneously in front of right shoulder on October 14, 1902, with 5 c. c. of a suspension of human culture F T. No marked disturbance of the health of the animal as a result of the inoculation could be observed. A tumor developed at the point of injection and persisted until June, 1903, when the animal was tested with tuberculin and gave a slight reaction. On July 23, 1903, the calf was killed. The only tuberculous lesions which could be found at autopsy were situated in the subcutaneous tissues at the point of injection.

Record of calf No. 291.—About 6 months old; no reaction from tuberculin test. On October 14, 1902, injected subcutaneously in front of right shoulder with 5 c. c. of a suspension made from human tubercle culture F L. The record of this animal is quite similar to that of calf No. 290. A tumor formed at the point of inoculation, but the health of the calf remained good. When tested with tuberculin on June 30, 1903, a slight reaction was obtained. The calf was killed on July 23 and examined postmortem. The only lesions found were situated in the subcutaneous tissues at the point of injection.

Human cultures F T and F L evidently did not possess sufficient pathogenic power to cause the infection of these two calves after subcutaneous injection.

Record of calf No. 284.—Red-and-white heifer calf, about 13 months old. Tested with tuberculin December 13, 1902, without reaction. January 24, 1903, injected subcutaneously in front of right shoulder with 5 c. c. of a suspension of bovine tubercle culture C No. 81. The injection was followed by the usual local swelling and enlargement of the prescapular gland. The animal in the course of two months failed somewhat in general condition, the respiration became slightly accelerated, and the local lesions persisted. On April 10, 1903, the general condition of the calf was poor and the animal was killed and examined postmortem.

Autopsy: At seat of injection on right side of neck there was an abscess about 3 by 4½ by 2 inches in size; below the abscess the prescapular gland was greatly enlarged and very firm. Lungs were sprinkled throughout with tubercles, which were more numerous in the anterior portions; these tubercles presented a minute pearl-gray center surrounded by a zone of pale-pink edematous tissue. Liver contained a few necrotic foci, which were visible on the surface. Mediastinal glands enlarged. Spleen contained tuberculous foci. Intestines contained numerous worm nodules; no mesenteric disease; a few tubercles, beginning pearly disease, on the omentum over paunch, and a few small tubercles were also found on the costal pleura. (See Pls. XXII and XXIII.)

Microscopic examination: Lung—The sections presented tubercles of varying size which contained giant cells and a few tubercle bacilli. Spleen showed extensive tubercle formation with giant cells and scattered tubercle bacilli. The sections from the liver and kidney showed no lesions.

Record of calf No. 223.—Tested with tuberculin without reaction. Age about two and one-half months. On November 2, 1901, this animal was injected subcutaneously with 10 c. c. of a suspension of bovine culture III (Smith). On January 21, 1902, and April 18, 1902, reactions after tuberculin injections were noted. On October 2, when the animal was killed, its general condition was excellent. At the seat of injection there were embedded small abscesses containing a soft, cheesy material. The shoulder glands on the side of infection, both deep and superficial, were enlarged and sprinkled with necrotic foci. The mediastinal glands contained numerous necrotic foci. No other lesions of any kind were present.

This animal showed, therefore, after eleven months, very much less evidence of tuberculosis than was found after six weeks in calves which received subcutaneous injections of material from tubercle cultures isolated from children.

TABLE V.—*Subcutaneous inoculations of calves.*

Material used.	Dose. c. c.	Number of animal.	Age of animal.	Date of inoculation.	Result of inoculation.
Tuberculous human lung and intestine.	1 piece of each.	Calf No. 250[a]	1 year...	Apr. 12, 1902	Killed Oct. 1, 1902.
Human culture C No. 4.	5	Calf No. 286[b]	6 mos...	Oct. 13, 1902	Killed Nov. 14, 1902, when in dying condition.
Human culture E T...	5	Calf No. 288[c]	....do...	.....do.......	Killed Dec. 19, 1902, in fair condition.
Do	5	Calf No. 285[d]	13 mos..	Jan. 24, 1903	Killed Apr. 28, 1903, condition poor.
Human culture D T...	5	Calf No. 287[e]	6 mos...	Oct. 13, 1902	Killed Dec. 19, 1902, condition fair.
Human culture G D...	6½	Calf No. 221[f]	18 mos..	Sept. 23, 1902	Still living, condition excellent.
Human culture F T...	5	Calf No. 290[g]	6 mos...	Oct. 14, 1902	Killed July 23, 1903, after tuberculin reaction.
Human culture F L...	5	Calf No. 291[g]	....do...	.....do.......	Do.
Bovine culture III	10	Calf No. 223[h]	2½ mos..	Nov. 2, 1901	Killed Oct. 2, 1902, condition excellent.
Tissue from monkey No. 1, inoculated with bovine III.	Small piece.	Calf No. 226[i]	1 mo....	.....do.......	Killed Oct. 6, 1902, condition poor.
Bovine culture C No. 81	5	Calf No. 284[j]	13 mos..	Jan. 24, 1903	Killed Apr. 10, 1903, condition poor.

The following footnotes show the condition of the calves after death:

[a] Tuberculosis of superficial lymph glands, and of the pulmonary and diaphragmatic pleuræ.

[b] The autopsy disclosed a severe generalized tuberculosis.

[c] Autopsy revealed lesions of a generalized tuberculosis.

[d] Generalized tuberculosis. Not so extensive as in case of calf No. 288.

[e] Glands adjacent to point of inoculation were tuberculous.

[f] Animal tested with tuberculin June 30, 1903, and did not react.

[g] No lesions except abscess at point of inoculation.

[h] Abscesses at point of inoculation. Shoulder glands on same side and mediastinal glands tuberculous. No other lesions.

[i] Tuberculosis of lungs, spleen, mediastinal, axillary and shoulder glands.

[j] Generalized tuberculosis.

Record of calf No. 226.—About 1 month old. Given tuberculin test without reaction. November 2, 1901, injected subcutaneously back of left shoulder with tuberculous tissue from monkey No. 1, which died as a result of inoculation with bovine III culture. The calf was tested with tuberculin on the following dates, each time giving a good reaction—January 21, February 27, April 18, and June 26, 1902. Killed October 6, 1902, and examined postmortem, Autopsy: At seat of injection a group of minute necrotic foci surrounded by thick connective tissue walls, the usual injection lesion produced by bovine tubercle germs. There were numerous minute foci of tuberculosis in the mediastinal glands; entire lung sprinkled with small tuberculous foci; the shoulder and axillary glands were tuberculous; numerous nodules of disease in the spleen; other organs and glands not affected. Two guinea pigs inoculated subcutaneously with a diseased fragment from the spleen of this calf died of generalized tuberculosis.

The widespread lesions found in this calf would seem to indicate an increase in the virulence of bovine III culture by passage through the monkey, inasmuch as a pure culture of the same organism failed to produce generalized tuberculosis in calf No. 223. Without more experimental evidence upon this point, however, we can not regard such an increase in virulence as definitely established.

MISCELLANEOUS ANIMAL EXPERIMENTS.

Record of calf No. 254.—Age, about 7 months. February 27, 1902, tested with tuberculin without reaction. March 7, 1902, injected intraabdominally with 5 c. c. of human sputum containing very many tubercle bacilli; also many other bacteria, staphylococci, etc. Within three weeks after injection the animal appeared to be unwell, appetite was poor, and there was considerable tenderness surrounding the point of injection. On May 1, 1902, the animal reacted to a tuberculin test, and declined in condition from that time on, and was killed on September 23, 1902.

Autopsy: On opening the abdominal cavity the left wall was found to be thickly studded with minute white elevations, varying in size from mere points to about one-eighth inch. Among these elevations were a few which had necrotic centers; similar but less numerous lesions on the omentum, the surface of the rumen, the abdominal and thoracic surfaces of the diaphragm, and on the mesentery; the lesions had very much the appearance of the beginning of pearl disease (see Pl. XX). A few necrotic foci were found in the tissue of the liver near the convex surface. The liver and the stomachs were bound to the diaphragm by means of firm bands of white connective tissue, which were studded with white elevations of the kind already described. The surface of the spleen was marked with similar elevations somewhat larger than in other regions. One cheesy nodule, about 1 inch in diameter, in the abdominal cavity near the duodenum; this nodule on section discharged a thick, granular pus. The walls of the abscess were moderately thick. Lung—The entire cephalic, two-thirds of the ventral, and one-fourth of the principal lobes on both sides were solidified, and of a pale-red color; the solidified areas were sprinkled with nodules, varying in size from one-sixteenth to one-half inch, which on section were found to be dilatations of the bronchial tubes filled with thick viscid mucus. The abdominal and thoracic glands were all enlarged and edematous, but showed no other lesions.

Guinea pigs inoculated with fragments of lung and of a nodule on the peritoneum died of generalized tuberculosis. Calf No. 276, injected with material from the peritoneum of calf No. 254, did not contract tuberculosis.

Calf No. 254 evidently contracted tuberculosis as a result of the injection with human sputum. The disease was not virulent in character, but was plainly progressive. The failure of calf No. 276 to contract the disease when injected with tuberculous tissue from calf No. 254 may have been due to the fact that it received the tubercle bacilli free from other organisms, whereas calf No. 254, which was injected with sputum, received a mixture of tubercle bacilli with various other microorganisms. In view of the fact that in calf No. 254 the tubercle bacilli invaded the lung and the costal pleura after intraabdominal injection, we consider this as a successful transference of human tuberculosis to cattle, although the human tubercle bacilli were aided possibly in their struggle with the resisting powers of the calf by other microorganisms.

Record of steer No. 242.—About 20 months old. The animal was drenched with bovine tuberculous material, obtained from cases of spontaneous tuberculosis in cattle, on January 10, 11, 13, and 21, 1902, and on February 17, 18, and 26 of the same year. Tested with tuberculin a positive reaction was obtained. On October 6, about 9 months after the first drenching, this animal was killed. A few small foci of a tuberculous character were found in the mediastinal and in the lymph glands at the entrance of thorax; otherwise there was no evidence of tuberculosis.

Record of heifer No. 237.—About 2½ years old. November 7, 1901, tested with tuberculin without reaction. This animal was then fed or drenched with tuberculosis material at varying intervals during a period of 6 months, as follows: November 22, 1901, fed with bran mixed with some tuberculous nodules from a human lung. December 23, 1901, a suspension was made in water of several tuberculous nodules from a human liver; a pint of this material was introduced into the stomach of the calf. December 26, 1901, drenched with a pint of a watery suspension of human tuberculous material, together with some serous fluid from the same case of human tuberculosis. January 8, 1902, drenched with a suspension of a tuberculous human liver. February 11, 1902, a suspension of tuberculous human lung in about 1 gallon of water, with about 50 c. c. of tuberculous human sputum, from adults suffering from pulmonary tuberculosis was introduced into the animal's stomach through a rubber tube. February 27, 1902, a tuberculin test showed no reaction. On March 4, 1902, the calf was drenched with a watery suspension of a portion of a tuberculous human lung. March 7, 1902, about 100 c. c. of tuberculous human sputum was fed to the calf through a rubber tube. About half of the sputum was derived from the same source as that used for the injection of calf No. 254; the other half was obtained from the case that furnished the material from which culture F L was obtained. Both contained large numbers of tubercle bacilli. April 5, 1902, a tuberculin test failed to give a reaction. On April 12, 1902, the heifer was drenched twice with tuberculous material of human origin; the first time it received a suspension of 8 to 10 cubic inches of a tuberculous human lung in water; at the second drenching, an hour later, it received a suspension of tuberculous intestines and mesenteric glands from a child, the latter material being derived from the same source as was culture C No. 4, the culture proving quite virulent for calves when injected subcutaneously. On May 13, 1902, a considerable amount of human tuberculous material (consisting of portions of the lung, liver, spleen, and kidney from a case of generalized tuberculosis) suspended in water was fed to the animal. May 19, 1902, about 8 or 10 cubic inches of a tuberculous human lung and mesenteric glands were cut into small fragments and mixed with water and fed to the calf. On June 26, 1902, tested with tuberculin without reaction.

The general condition of this animal remained excellent; it was killed on October 28, 1902, and the autopsy revealed no trace of tuberculosis. It must be said with regard to the material used for feeding the animal that none of it was proved to possess noticeable pathogenic virulence for cattle upon subcutaneous injection, with the exception of that marked C No. 4. Previous to receiving the virulent material, however, many feedings of a tuberculous virus of a low degree of virulence had been given, and there is a possibility that a certain amount of resistance to tuberculosis had been acquired in this way; in any case one feeding experiment of this character can not be considered as in any way decisive, the individual resistance of the animal being a quantity which must always be reckoned with.

Record of sheep No. 41.—January 29, 1902, tested with tuberculin without reaction. July 19, 1902, injected 10 c. c. of human tubercle culture No. 50 into right jugular vein. As a result of this injection the animal developed a severe respiratory disturbance and lost considerably in condition. At times it seemed to improve, but failed again and gradually became very emaciated. On January 6, 1903, the sheep was killed and examined postmortem.

Autopsy: Lung—The pleura showed numerous patches of thickening which in many places looked like fibrinous neoplasms of a shreddy character, and which constituted in some cases adhesions between the costal and pulmonary pleuræ; the lung tissue was sprinkled with nodules of a necrotic tuberculous character varying in size from one-sixteenth to one-half inch. (See Pl. XXIV.) Mediastinal gland tuberculous; some white points in the liver, kidney, and spleen; the general appearance was that of a tuberculosis which had its origin in the lung, spreading from this organ and finally producing a generalized miliary tuberculosis.

TABLE VI.—*Miscellaneous animal experiments.*

Animal.	Material used.	Method of administration.	Age of animal.	Date of exposure to infection.	Result.
Calf No. 254[a] ..	Tuberculous human sputum.	Intraabdominal (5 c. c.).	7 mos...	Mar. 7, 1902	Killed Sept. 23, 1902.
Heifer No. 237[b]	Tuberculous human tissue and sputum.	By mouth....	2½ years.	Nov. 22, 1901	Killed Oct. 28, 1902.
Steer No. 242[c] .	Tuberculous bovine tissue.	.....do........	20 mos..	Jan. 10, 1902	Killed Oct. 6, 1902.
Sheep No. 41[d] ..	Human tubercle culture 50.	Intravenous (10 c. c.).	Old ewe.	July 19, 1902	Killed Jan. 6, 1903.

The following footnotes show the condition of the animals after death:

[a] Tuberculosis of peritoneum, lungs, and pleuræ.

[b] No tuberculosis.

[c] A few small tuberculous foci in mediastinal and anterior thoracic glands. No other lesions.

[d] Generalized tuberculosis.

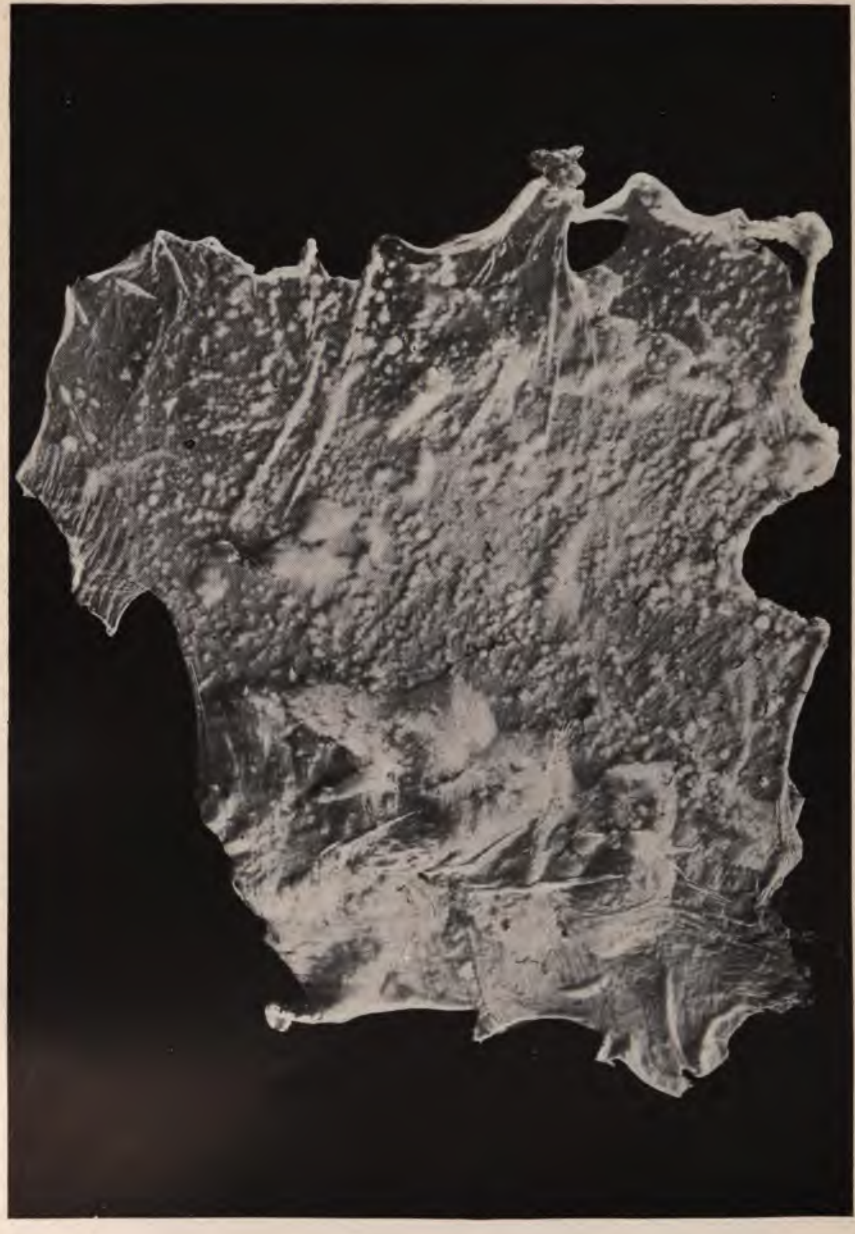
As will be seen from the foregoing records, several drenching or feeding experiments with cattle were made both with human and bovine tuberculous material. At the time the animals were killed the human material had not caused any disease, while the bovine material had produced slight results. When we compare the disease produced by bovine III culture, which had been grown in the laboratory of the Bureau for a number of generations, with that produced by bovine culture C No. 81—the culture recently isolated—there seems to be almost as great a difference in virulence between the two as there is among the various cultures of human origin.

DISCUSSION OF THE CATTLE EXPERIMENTS.

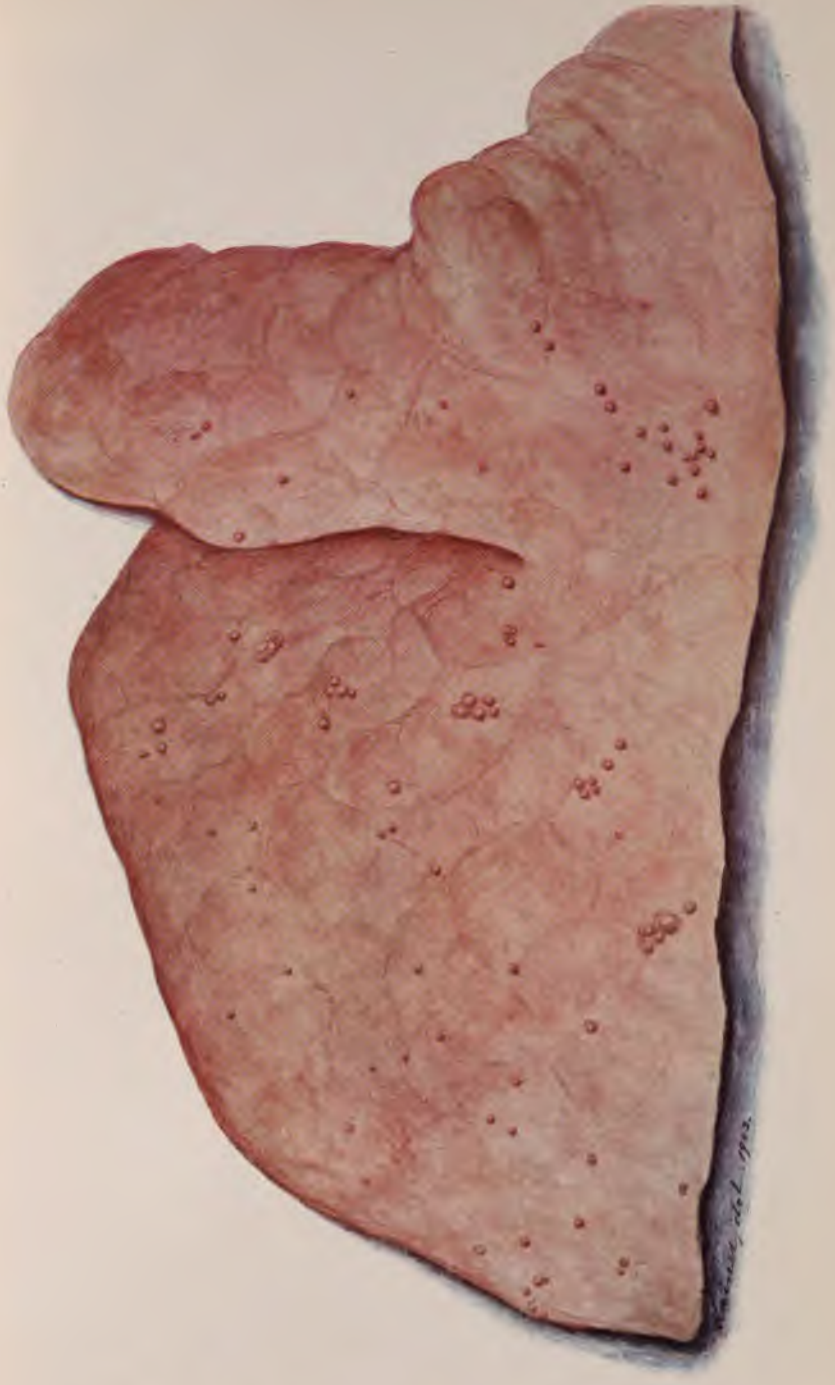
We isolated in all nine fresh tubercle cultures from as many different cases of human tuberculosis. Five of these cultures were obtained from adults and four from children. One calf was injected intravenously with each of the cultures, but owing to the fact that the microscopic examination of the organs of calf No. 265, injected with human culture D T, revealed the presence of large numbers of a microorganism differing from the tubercle bacillus, we will not take this case into account in determining the percentage of positive results. An examination of the record of calf No. 287, injected subcutaneously with the same culture—D T—indicates that this culture possesses distinct though rather feeble pathogenic power for cattle. If the record of calf No. 287 be compared with that of calf No. 223, injected subcutaneously with bovine culture III, it will be seen that, assuming the resisting powers of the two calves to be equal, human culture D T is nearly, if not quite, as virulent for calves upon subcutaneous injection as bovine culture III, and this bovine culture, upon intravenous injection, produced an infection of the lungs and lymphatic glands. Reasoning in this fashion, we are inclined to believe that human culture D T was the chief cause of the lesions found in calf No. 265, but owing to the element of uncertainty, which can not be overcome, this animal will not be considered among the intravenous injections.

Eight calves were injected intravenously with as many different cultures of tubercle bacilli of human origin, five being obtained from adults and three from children. Of the eight cultures, two, or 25 per cent, produced a fatal generalized tuberculosis. The two that produced fatal disease in calves were both derived from children; therefore two out of three of the cultures from children were quite as virulent for calves as the bovine tubercle bacillus.

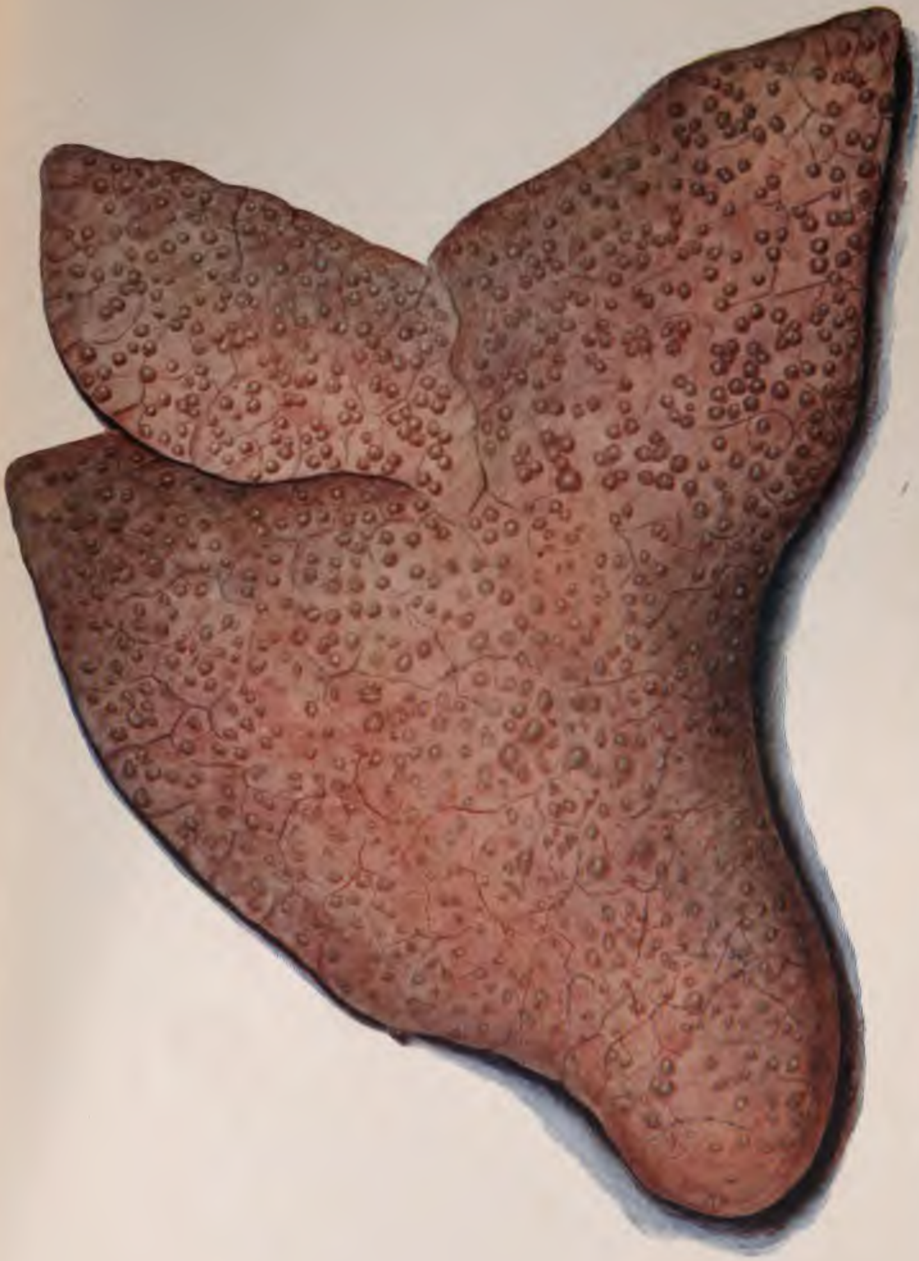
It was not thought necessary to inject calves subcutaneously with the cultures which gave little or no evidence of pathogenic properties when injected intravenously. Six of the most virulent human cultures were therefore selected for the subcutaneous injections. As indicated in Table V, seven calves were injected subcutaneously with the six cultures, and one calf (No. 250) was injected with human tuberculous tissue obtained from the same source as one of the cultures (C No. 4). Three of the six cultures used were derived from adults and three from children. The results of these injections may be summarized as follows: One culture failed to produce any lesion persisting for as long a period as 9 months; two produced a localized abscess at the point of injection; a fourth culture produced a local lesion and the disease extended to the neighboring lymph glands. The two remaining cultures brought about a generalized tuberculosis in the calves injected with them. Taking into account, then, the whole number of human cultures isolated, we find that two out of nine, or 22.2 per cent, produced a generalized tuberculosis after subcutaneous injection. A third culture, D T, must be considered as infectious for cattle, as the disease within 2 months from the time of injection extended from the point of inoculation to the adjacent prescapular gland, and through that or some other channel to the deeper gland just inside of the thorax. We can then revise



PERITONEUM FROM CALF No. 254, SHOWING THE LARGE NUMBER OF TUBERCLES PRODUCED BY THE INTRAPERITONEAL INJECTION OF HUMAN TUBERCULOUS SPUTUM.

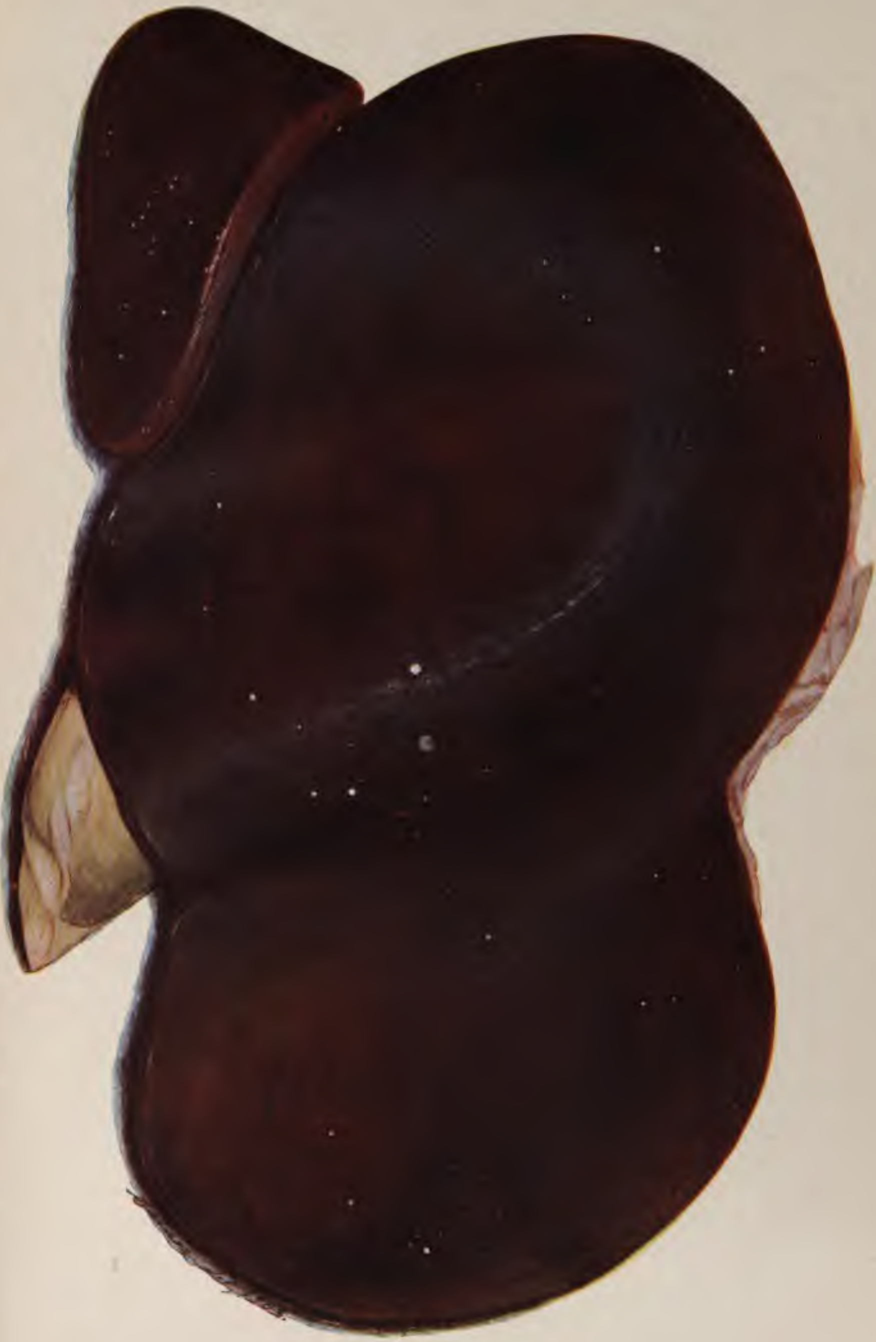


NATURAL BOVINE TUBERCULOSIS IN LUNG OF COW.



Lung, Calf 284. Subcutaneous inoculation with pure culture bovine tuberculosis No. 81.

Plate XXIII.



Liver, calf 284. Subcutaneous inoculation with pure culture bovine tuberculosis No. 81.

the figures just given, since out of nine human cultures isolated, three, or 33⅓ per cent, produced tuberculosis in cattle after subcutaneous injection. These three virulent cultures were all obtained from children, so that out of four cultures derived from cases of generalized tuberculosis in children three were capable of bringing about infection in cattle.

It will be remembered that in the summary of the intravenous injections it was stated that two out of three of the cultures from children produced tuberculosis in calves, while after subcutaneous injection we state that three out of four produced infection. This discrepancy is due to the fact previously explained that a mixed infection appeared to have taken place in the animal injected intravenously with culture D T, and for this reason the injection with that culture was thrown out.

So far as our experiments upon cattle are concerned, therefore, we must conclude that tubercle bacilli of various degrees of virulence for cattle may be obtained from human sources—some quite as virulent as the tubercle bacilli known to be of bovine origin and others less so.

The results of our experiments also lead us to conclude that there is no essential difference between tubercle bacilli derived from bovine sources and those derived from man. In fact, we know of no character possessed by bovine tubercle bacilli which may not be possessed by tubercle bacilli of human origin. The two most virulent human tubercle cultures described in this bulletin can not be distinguished from the classical bovine type either with regard to their cultural characters or their pathogenic power for cattle and other animals.

Dr. Theobald Smith has been the chief advocate for a racial distinction between bovine and human tubercle bacilli, although he does not deny the infectiousness of bovine tubercle bacilli for man. On the contrary, he considers those cultures of human tubercle bacilli which correspond culturally and in respect to their pathogenic powers with the ordinary bovine tubercle bacillus as being originally of bovine origin.

While we believe firmly that tubercle bacilli of bovine origin may infect human beings, we can not accept the theory that tubercle bacilli derived from man are necessarily of bovine origin because they possess characters of the ordinary bovine bacillus. In other words, in regard to those cases of human tuberculosis from which bacilli virulent for cattle are obtained, it must be shown first of all that the individuals in question became infected through tuberculous meat or milk. The possibility of the infection having been derived from cattle always exists, but in our opinion the biological characters of the infecting organism are not sufficient to show that meat or milk was the source of the disease, and in like manner a tubercle bacillus of low virulence obtained from cattle should be considered to be of bovine origin unless there is some evidence of infection from other sources. The fact that certain tubercle bacilli derived from man resemble the majority of bovine bacilli is to our mind evidence of the unity of the two races.

EXPERIMENTS UPON MONKEYS.

In addition to the investigations made to determine the extent to which tubercle bacilli of human origin are infectious for cattle, the intimately related question whether tubercle bacilli of bovine origin are infectious for man was approached as closely as possible by a series of experiments with monkeys.

It is a generally admitted zoological fact that man stands in closer relationship to the quadrumana than to other animals. With this view accepted, we may reasonably assume that apparently similar disease-producing microorganisms found in man and cattle, the identity of which has been questioned, are practically the same in their pathogenic significance if they produce identical affections in monkeys.

Of the monkeys used in our experiment one was a Cebus, two belonged to the genus Rhesus, and four were baboons. Two tubercle cultures were used, one—No. 50—of human origin, which had been under cultivation for a long time at the laboratory and was virulent for guinea pigs, and one bovine culture—III.

Four of the monkeys received injections of bovine tubercle culture; two received injections of human tubercle culture, and one was fed milk containing bovine tubercle bacilli. No cow could be found with a tuberculous udder which had become infected in the natural way at the time the feeding experiment was made, and so the milk was obtained from a cow whose udder was injected with culture bovine III. The milk from the udder-injected cow showed the presence of tubercle bacilli on microscopic examination, and on injection into guinea pigs caused fatal, generalized tuberculosis.

The monkeys were confined in large cages, each of which was supplied with perches and a partly closed sleeping compartment to which the animal could retire at will. The cages were placed in a one-roomed, properly heated, well-lighted and ventilated house, which was guarded during cold weather against sudden changes of temperature by a small vestibule with inner and outer doors. Both the cages and the house were specially constructed for this experiment and had not been used previously for any other purpose.

Record of monkey No. 1.—Female baboon, in excellent condition, tested with tuberculin without reaction, kept under observation about two weeks and showed no symptoms of disease; weight 8 pounds 9 ounces. September 12, 1901, injected subcutaneously, left side, about 1 inch below udder, with 1 c. c. tubercle culture bovine III.

A firm tumor at once developed at the seat of injection, which gradually increased in size, softened, broke open, and discharged a creamy, gray, pus-like substance, and formed, by October 4, a deep ulcer, 1 by ½ inch in area, with a thickened, rounded, raised border. The skin about the ulcer became generally thickened and detached from the subcutaneous structures over a diameter of 2½ inches. The monkey spent much time fingering and picking the wound, which was washed with weak solution of carbolic acid and covered with a thin layer of powdered chalk and alum. The axillary lymph gland on the side of injection increased greatly in size and was clearly visible as a tumor under the skin when the monkey's arm was drawn upward. On October 8 the ulcer at the seat of injection was almost circular, 1½ inches diameter, and its surface was covered by a thin layer of thick, gray pus. The enlarged axillary gland measured 1 by ¾ by ½ inch, and was firm and nodular to the touch. On October 12 the weight of the monkey was 7 pounds 15 ounces, and on October 26 this had fallen to 7 pounds.

The general condition of the monkey, beginning a few days after the injection until October 30, 1901, on which date she was chloroformed and examined postmortem, became gradually worse. On October 29 the following record was made: Monkey has been growing constantly weaker and now is so weak that she can barely sit with her body in an erect position. She is drowsy, keeps her eyes closed, and rests her head on her hands in a very human attitude, and refuses all nourishment excepting a little fruit. The next day, on which she was killed, she was noticeably weaker and practically in a dying condition.

Autopsy: At the seat of injection a large ulcerated area, about 1½ inches in diameter. The pleural cavity contains a viscid, serofibrinous exudate, by means of which the costal and pulmonary pleuræ are bound together. The lung is thickly sprinkled with opaque, yellowish white areas, of a cheesy appearance, the diameter of which varies from 1 mm. to about 2 cm. The several lobes of the lung are adherent to each other and the lung tissue is firm and airless. Pericardium distended with clear, serosanguinous fluid. Heart—Near the apex of the left ventricle, in the muscle, is an opaque, white area about 2 mm. in diameter. Liver apparently enlarged and mottled with numerous opaque, white areas from 1 to 5 mm. in diameter. Spleen apparently enlarged and sprinkled with opaque, dirty-white areas, which have a cheesy appearance and vary in diameter from 1 mm. to 1 cm. Kidneys pale and studded with opaque, white areas about 1 mm. diameter. The mediastinal, axillary, and mesenteric lymph glands are enormously enlarged, and are hard and cheesy.

The mesentery is sprinkled with opaque, white areas. The brain is normal in appearance, with the exception of a white focus 1 mm. in diameter embedded in the pia mater lying over the subfrontal sulcus.

Record of monkey No. 2.—Small female Cebus, in unthrifty condition, hair rough and soiled in places, tested with tuberculin without reaction; weight 2 pounds 1 ounce. September 12, 1901, injected subcutaneously, left side, about 1 inch below udder, with ½ c. c. of tubercle culture bovine III.

Condition as a result of the injection is similar to that described for monkey No. 1, in addition to which the mammary gland directly above the seat of injection is swollen and firm and the skin covering it, especially about the nipple, reddened. This animal gradually lost in condition, but remained fairly bright until the latter part of October. On October 12 its weight was 1 pound 14 ounces, on October 26 also 1 pound 14 ounces. On November 7 the following record was made: Weight 1 pound 12½ ounces; condition very poor and unthrifty; hair roughened and much soiled; mammary gland greatly swollen and the skin over same, especially about the nipple, intensely reddened; ulcer at the seat of injection 1 inch long and ¾ inch broad; appetite very poor. On November 22 the monkey was in a dying condition and was chloroformed and examined postmortem.

Autopsy: The animal is very much emaciated. At the seat of injection is a large raw, ulcerated area, about 1 inch in diameter, over which the skin has entirely disappeared; the edges of the skin surrounding the opening are somewhat everted. Lung sprinkled with grayish, translucent foci from 1 to 20 mm. in diameter, the centers of which are opaque and of a yellowish white color. Liver apparently normal. Spleen of a dark color and studded with opaque yellowish white areas from 1 to 3 mm. in diameter. Kidneys pale and contain a number of translucent areas about ½ mm. in diameter; the left kidney, on section, is found to contain a yellowish white, opaque, necrotic area about 3 mm. in diameter. Lymphatics—The axillary, mediastinal, and mesenteric glands are all enlarged and cheesy, and all, on section, show more or less softening and the presence of thick, white pus.

DESCRIPTION OF PLATE XXVI.

Sections of organs of monkey No. 3, indicating distribution of tubercle bacilli from subcutaneous inoculation with pure culture human tuberculosis No. 50. Stained with hematoxylin and carbol-fuchsin. Magnified 1,450 diameters.

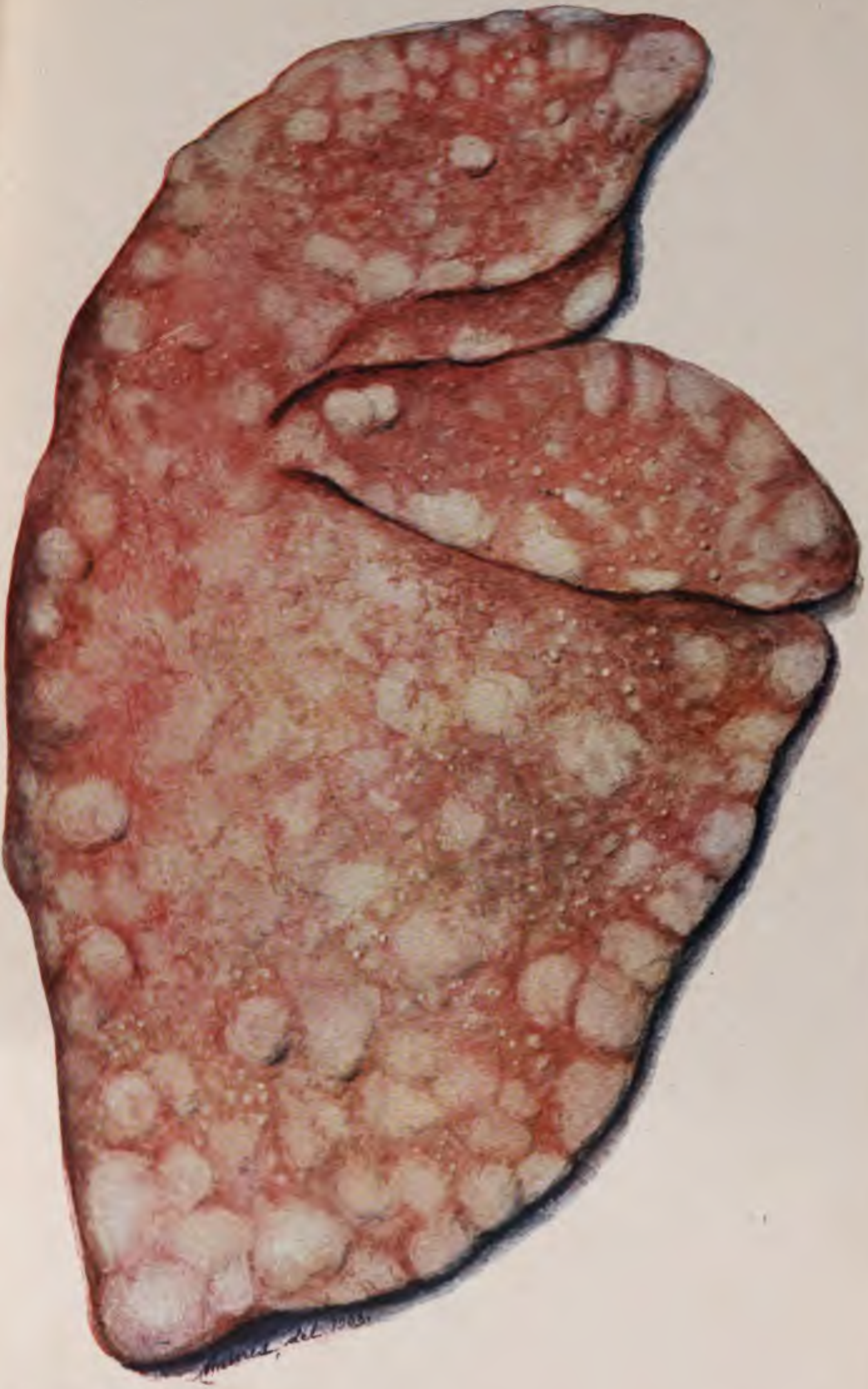
Fig. 1.—Section of lung.

Fig. 2.—Section of liver.

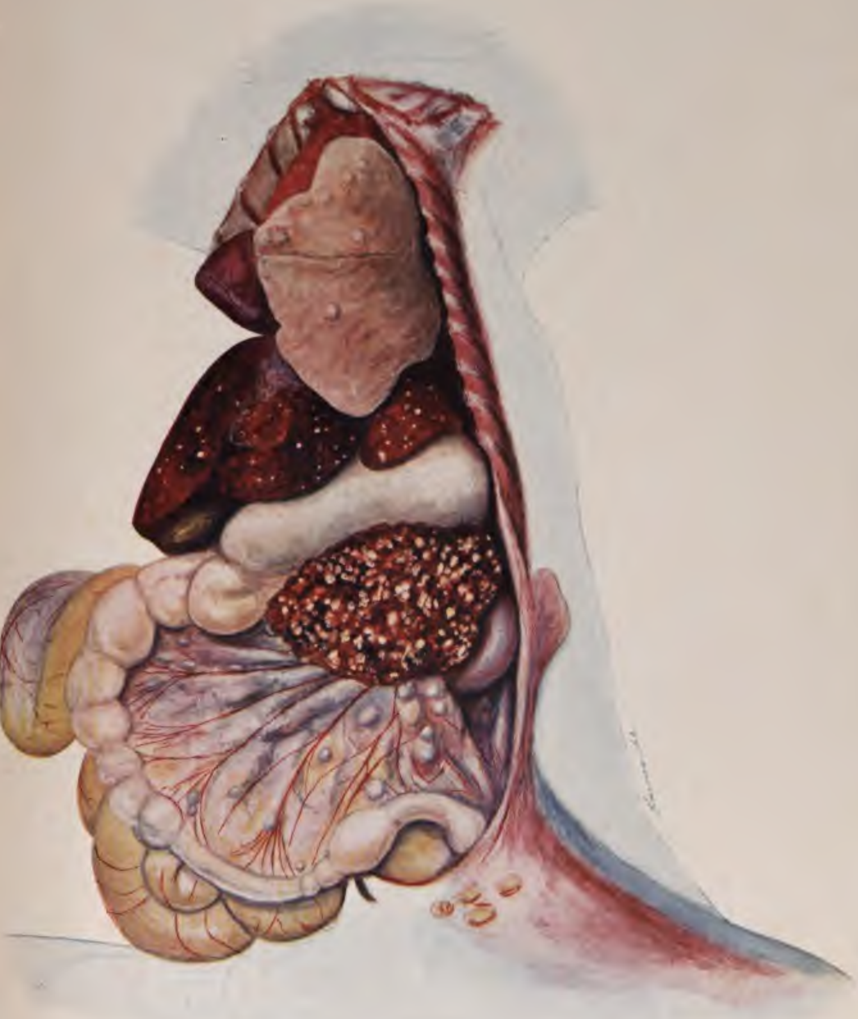
Drawing by W. S. D. Haines.

Bulletin No. 52, B. A. I.

Plate X



ung, Sheep 41. Intravenous inoculation with pure culture human tuberculosis No. 50.



Monkey No. 3. Baboon, subcutaneous inoculation with pure culture human tuberculosis No. 50.

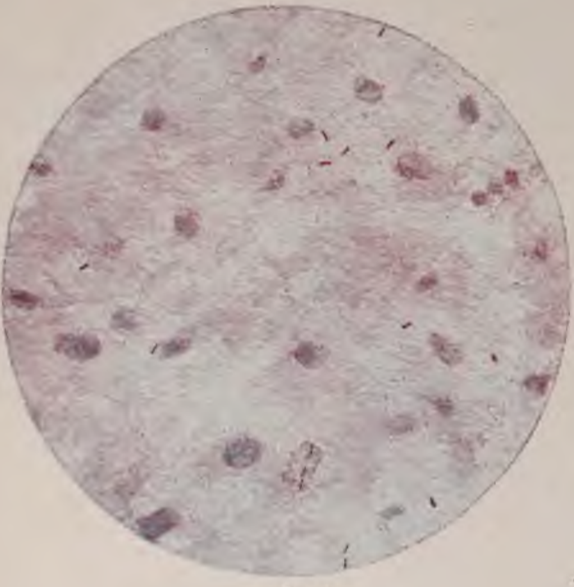


Fig. I.

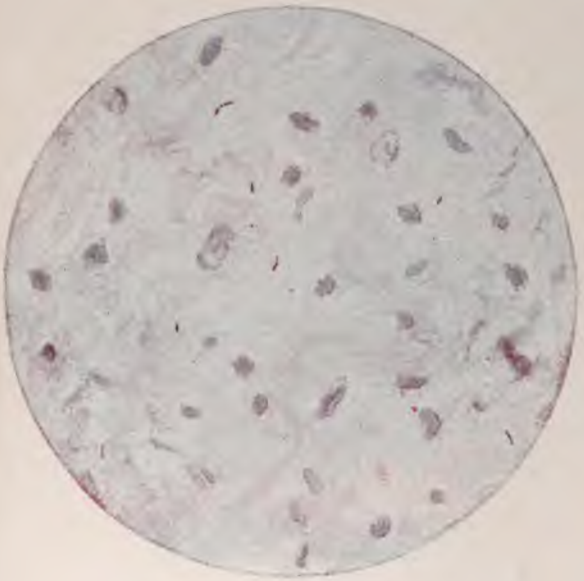


Fig. 2.

Tubercle bacilli in sections from Monkey No. 3, human tuberculosis No. 50.

Record of monkey No. 3.—Female baboon, in excellent condition, tested with tuberculin without reaction; weight 9 pounds 8 ounces. November 7, 1901, injected subcutaneously inside of right thigh with 1 c. c. of human tubercle culture No. 50.

November 20, at the seat of injection an ulcer, ½ by ¾ inch, has formed, in all respects similar to the ulcer described at the seats of injection of monkeys Nos. 1 and 2. The superficial inguinal gland near the seat of injection is greatly enlarged and very firm. From this time on the ulcer and inguinal gland gradually increased in size and the inguinal gland on opposite side showed some swelling. On December 4 the weight had fallen to 7 pounds 14 ounces, and the animal was depressed and had a severe cough which lasted until death. On December 18 the weight was 7 pounds 7 ounces. On December 28 the monkey was very drowsy, depressed, and weak, and had lost her appetite entirely, and was suffering with a diarrhea, the discharges of which were of a creamy consistency and a pale-yellow color. On December 30, being in practically a dying condition, she was chloroformed and examined postmortem.

Autopsy: General condition very poor; weight 6 pounds 15 ounces. An ulcer at seat of injection of such depth that the muscles of the thigh are exposed over an area 3 cm. in diameter; an abscess in the inguinal region, near the ulcer, about 2 cm. in diameter. Inguinal gland near seat of injection enlarged and tuberculous. Lung sprinkled with tubercles varying greatly in size. Spleen filled with caseous tubercles. Liver sprinkled with small white tubercles. Kidneys contained a few small tubercles. Mesenteric, mediastinal, and bronchial glands are enlarged and caseous. (See Pls. XXV and XXVI.)

Record of monkey No. 4.—Male baboon, in excellent condition, tested with tuberculin without reaction; weight 9 pounds 12 ounces. November 7, 1901, injected subcutaneously inside of right thigh with 1 c. c. bovine tubercle culture III (14).

November 20, an abscess, 15 mm. in diameter, has formed at seat of injection, from a small opening in which a thin, brown fluid is being discharged. The superficial inguinal gland near seat of injection is firm and appears as a tumor, about 1 cm. in diameter, under the skin. Weight of animal this date is 9 pounds 15½ ounces. December 4, weight 9 pounds 9 ounces. The lesion at seat of injection is now an ulcer, in all respects similar to the injection ulcers described in connection with monkeys Nos. 1, 2, and 3. The inguinal gland near seat of injection is greatly enlarged, the animal is dull, and suffers with paroxysms of coughing which last several minutes at a time. December 18, weight 9 pounds; monkey becoming weaker and showing practically the same symptoms observed during the last week of life in monkey No. 3—depression, weakness, drowsiness, cough, and diarrhea. December 23, in practically dying condition, chloroformed and examined postmortem.

Autopsy: An ulcer at seat of injection similar to the one described for monkey No. 3. The inguinal gland near this region is as large as a hen's egg, and tuberculous. Lungs congested and thickly sprinkled with opaque, yellowish white areas, of a cheesy character, varying in size from points to 1 cm. or more diameter. Liver closely sprinkled with opaque yellowish white, necrotic areas, from points to 1 mm. diameter. Spleen greatly enlarged and mottled; closely studded with raised, opaque, yellowish white areas, from 1 mm. to 1 cm. or more diameter; these areas, like those in the lung, are filled with softened, cheesy, necrotic material. Omentum is sprinkled with minute white points. Lymph glands show lesions of tuberculosis. (See Pls. XXVII and XXVIII.)

Record of monkey No. 5.—Male rhesus, in excellent condition, tested with tuberculin without reaction; weight, 5 pounds 11½ ounces. November 7, 1901, injected, subcutaneously, inside right thigh, with 1 c. c. human tubercle culture, No. 50.

The condition of this monkey, relative to the lesions at seat of injection and general constitutional symptoms, is so much like that described for monkeys Nos. 3 and 4 that a separate description would be superfluous. The monkey died December 21, at which time he weighed 4 pounds 1 ounce.

Autopsy: Lesion at seat of injection similar to that found in monkeys Nos. 3 and 4. Lungs—The upper or anterior lobe on the right side completely solidified, the lower portion of the corresponding lobe on the left side in a similar condition; the lungs as a whole show a sprinkling of translucent, grayish white areas, from 1 to 2 mm. diameter. Liver contains numerous small, opaque, yellowish white areas, varying in size from mere points to areas 1 and 2 mm. in diameter. Spleen dark in color, and closely covered with elevated, yellowish white areas from 1 to 10 mm. diameter. Lymph glands show enlargement and necrotic changes. The gland in inguinal region contains thick, creamy pus. (See Pl. XXIX.)

Record of monkey No. 6.—Female rhesus, in excellent condition, tested with tuberculin without reaction; weight, 5 pounds. November 7, 1901, injected, subcutaneously, inside of right thigh, with 1 c. c. bovine tubercle culture III.

November 20, a large fluctuating abscess has formed at seat of injection. December 4, the monkey is very sick and so weak that she can move about the cage only with considerable effort; her respiration is accelerated and labored. When she was caught to be weighed the abscess at seat of injection broke and discharged about 4 c. c. of creamy pus in which firm masses of necrotic tissue were held in suspension. The skin over the abscess is reddened and that surrounding it is swollen. Weight, 3 pounds 15 ounces. December 11, found dead; weight, 3 pounds 9 ounces.

Autopsy: Lung—The upper lobe on left side completely solidified; sprinkled throughout the organ are a few grayish white areas, about 1 mm. diameter. Liver apparently enlarged, and closely studded with small, opaque white areas, varying in size from points to 1 mm. in diameter. Spleen enlarged and closely sprinkled with raised, opaque white areas, varying from points to 2 mm. in diameter. The mesenteric glands are enlarged and show occasional yellowish white, cheesy areas. (See Pl. XXX.)

Record of monkey No. 7.—Female baboon, received at the experiment station January 30, 1902; tested with tuberculin without reaction February 13, 1902. General condition very good.

This monkey was fed with milk obtained from three cows, as follows: From February 21 to 25, inclusive, the milk of a cow which had received an injection of bovine culture III a month previously into the connective tissue which binds the posterior half of the udder to the body; from February 26 to 30, inclusive, the milk of a cow supposed to have a naturally infected udder; from May 22 to July 9, inclusive, the mixed milk of the two above cows; and from July 17 to November 10, inclusive, the milk of a cow which had received, on July 9, an injection of bovine tubercle culture III into the udder through the teats.

Careful microscopic examination of the milk of the first two cows, also the injection of guinea pigs from time to time with this milk, failed to demonstrate the presence of tubercle bacilli; while similar tests of the milk of the third cow showed tubercle bacilli under the microscope and caused fatal generalized tuberculosis in all the guinea pigs injected. Guinea pigs were injected from the last cow on the following dates: July 18, 19, 21, 22, 23, 24, 25, 26, and 28, and August 4, 7, 11, and 14, one guinea pig each day, with the exception of July 19, on which day six were injected. Six guinea pigs were also fed milk from this cow from August 16 to November 10, on which date they were killed, and three of them were found to be affected with tuberculosis.

The monkey received milk twice daily, about 120 c. c. at each feeding. Her general record is as follows: From February, 1902, to January, 1903, condition excellent. Retested with tuberculin without reaction on April 18, 1902. Weight on February 28, 1902, 9 pounds 9 ounces; on April 9, 10 pounds 1 ounce; and on July 21, 11 pounds 2 ounces.

In January, 1903, about 6 months after the feeding of the milk of the third cow began, and about 2 months after it was stopped, a perceptible loss in condition occurred. January 30, 1903, respiration accelerated and accompanied by a wheezing sound. February 3, the weight had fallen to 10 pounds. February 18 acted as though affected with headache. February 28, has a discharge from nostrils and is drowsy. March 14, is very much weaker and lacks appetite; discharge from nostrils continues. March 24, is very sick and weak; sits on the floor of cage with head thrown back; has a profuse discharge from nose, and refuses all food. March 26, died late in the afternoon; weight, 6 pounds 14 ounces.

Autopsy: Extremely emaciated. Lungs—Sprinkled over the pulmonary pleura are a number of tubercles from 1 to 8 mm. diameter, which have a gray hue. Many similar tubercles on the costal pleura, on which are also found tubercles with pedicles which greatly resemble the appearance frequently found in pearl disease of cattle. Liver contains a few white, sharply outlined areas, about 2 mm. diameter, and a large number of small grayish points scattered over its entire surface. Spleen is enlarged and dark in color, and scattered through it are a large number of caseous areas. Careful examination of the intestine failed to reveal disease. Guinea-pig injections and microscopic examination of the various organs demonstrated the presence of tubercle bacilli. (See Pl. XXXI.)

TABLE VII.—*Monkey experiments.*

Material used.	Method of administration.	Dose.	No. of monkey.	Date of inocculation.	Result of inoculation.
		c. c.			
Culture bovine III	Subcutaneous	1	1	Sept. 12, 1901	Killed Oct. 30, 1901. [a]
Do	do	½	2	do	Killed Nov. 22, 1901. [b]
Culture human No. 50	do	1	3	Nov. 7, 1901	Killed Dec. 30, 1901. [b]
Culture bovine III	do	1	4	do	Killed Dec. 23, 1901. [b]
Culture human No. 50	do	1	5	do	Died Dec. 21, 1901. [c]
Culture bovine III	do	1	6	do	Died Dec. 11, 1901. [c]
Tuberculous milk (culture bovine III).	By mouth	([d])	7	[d]July 17, 1902	Died Mar. 26, 1903. [c]

[a] In dying condition when chloroformed. Generalized tuberculosis.
[b] In dying condition when chloroformed. Lesions of generalized tuberculosis.
[c] Lesions of generalized tuberculosis.
[d] Fed twice daily until November 10, 1902.

It will be well for us to state that the tuberculous character of the lesions in the monkeys used in the experiments was confirmed in all cases by microscopic examination or by guinea-pig injection, or by both.

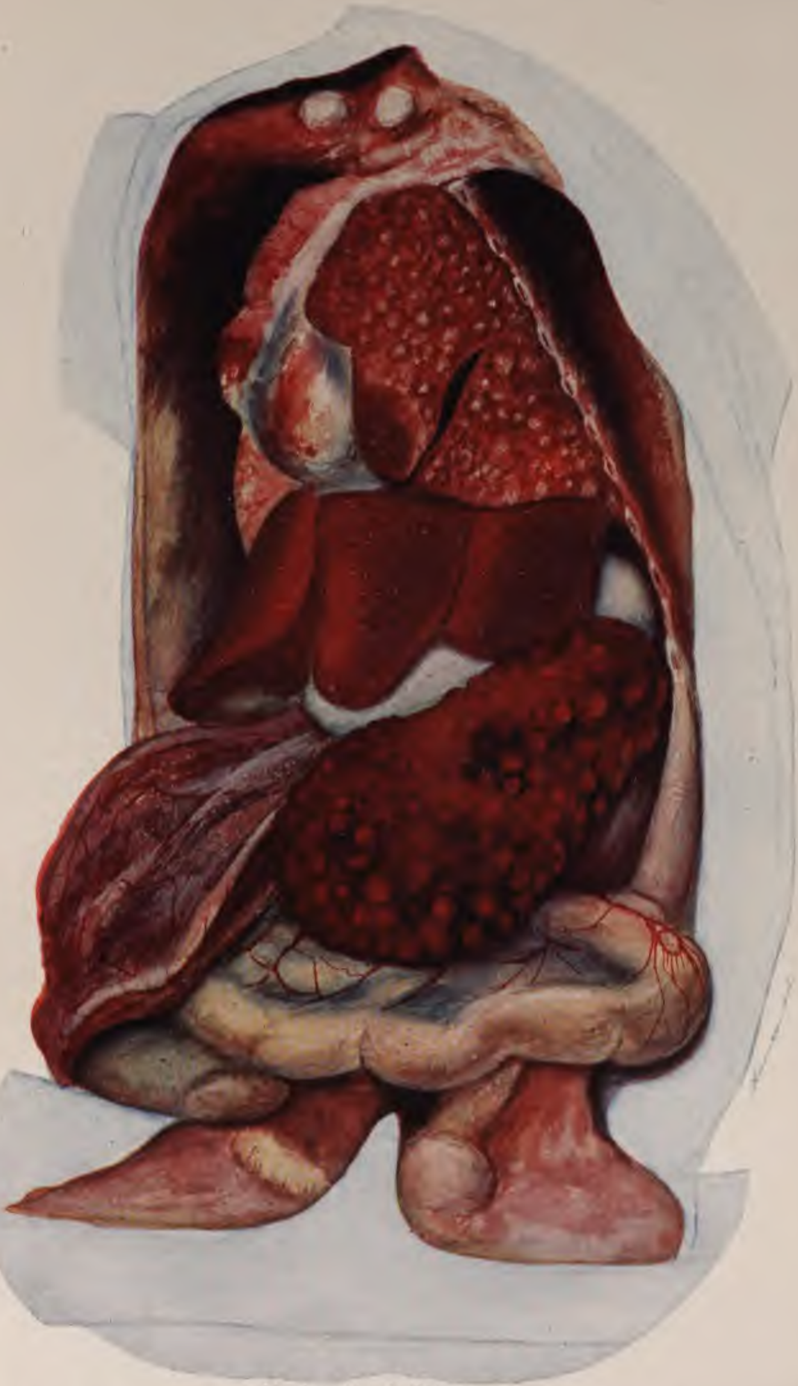
DESCRIPTION OF PLATE XXVIII.

Sections from monkey No. 4, indicating the distribution of the bacilli in the diseased organs resulting from subcutaneous inoculation with bovine culture III. Stained with hematoxylin and carbol-fuchsin. Magnified 1,450 diameters.

Fig. 1.—Section from liver.

Fig. 2.—Section from spleen.

Drawing by W. S. D. Haines.



Monkey No 4. Baboon,
subcutaneous inoculation with pure culture bovine tuberculosis No. III.

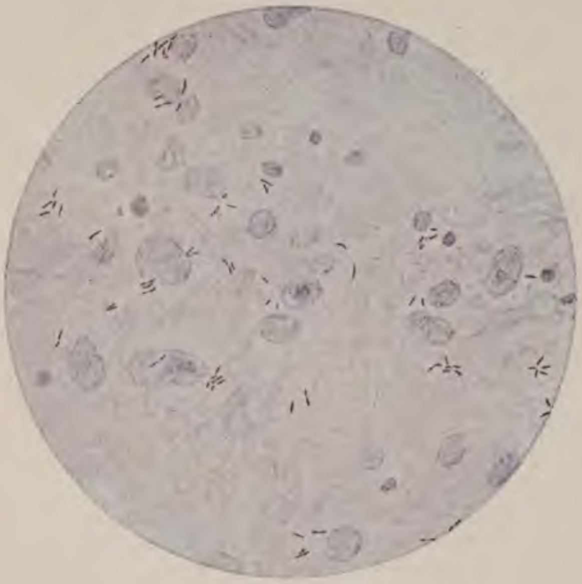


Fig. 1.

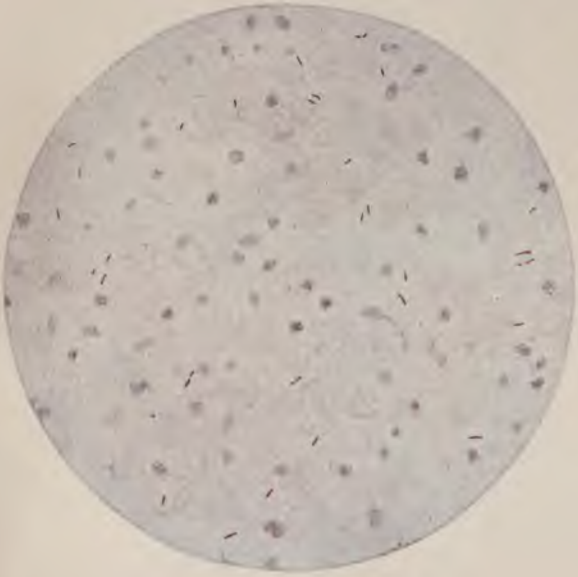
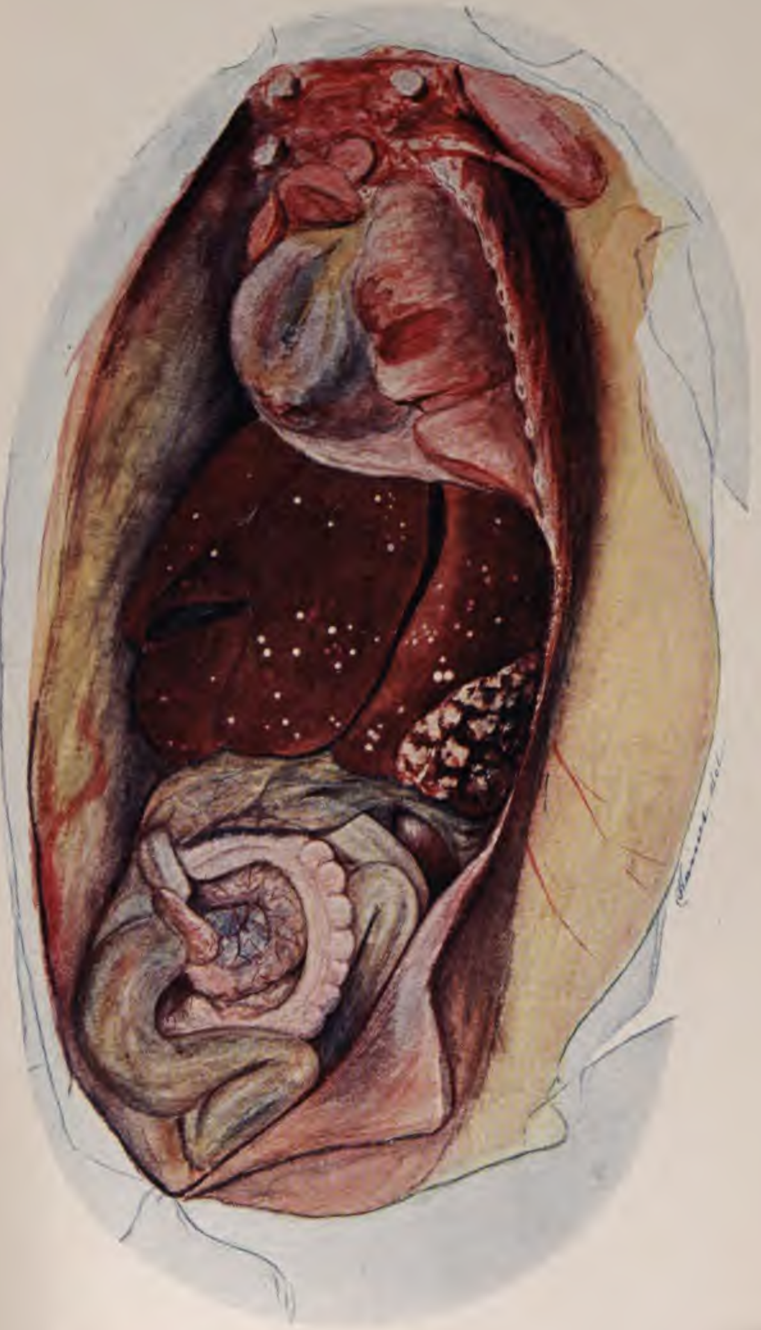
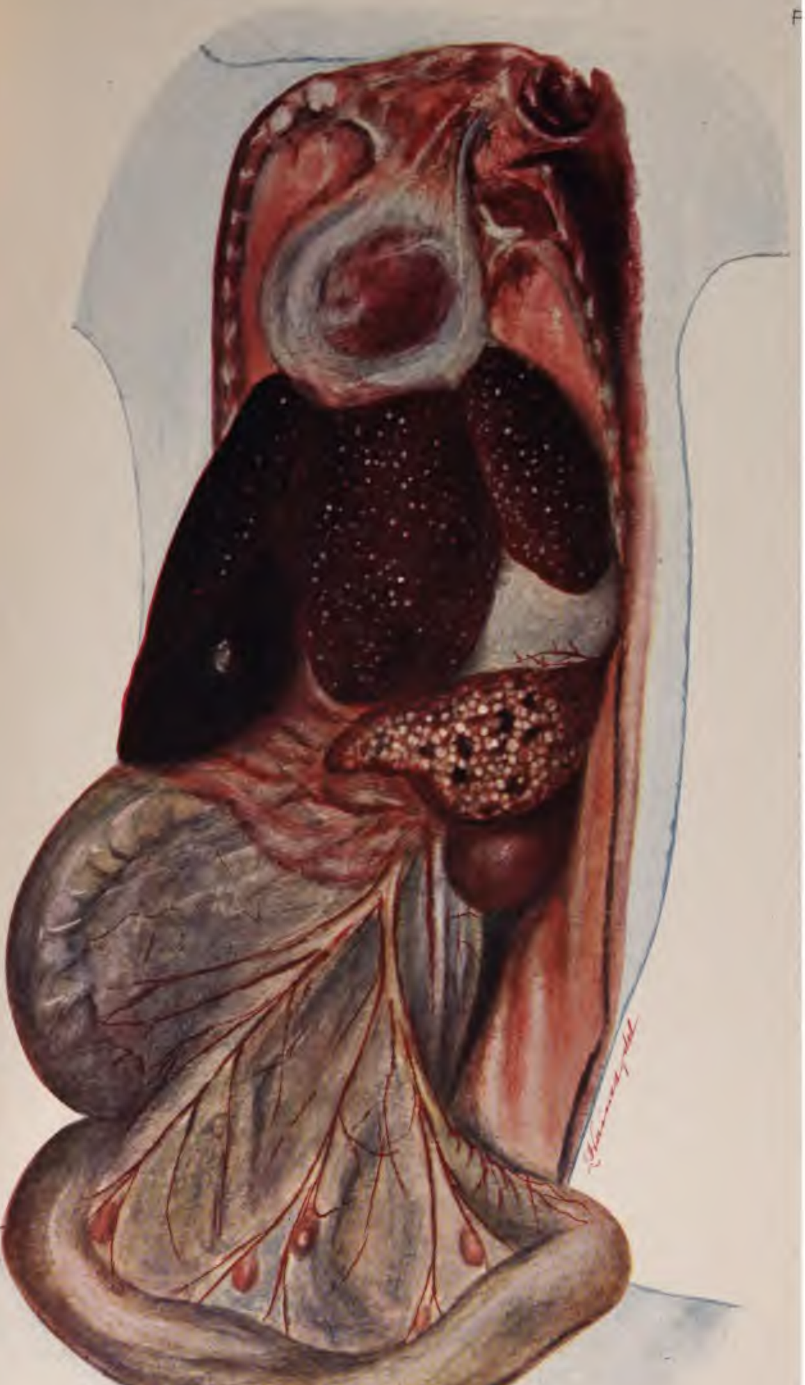


Fig. 2.

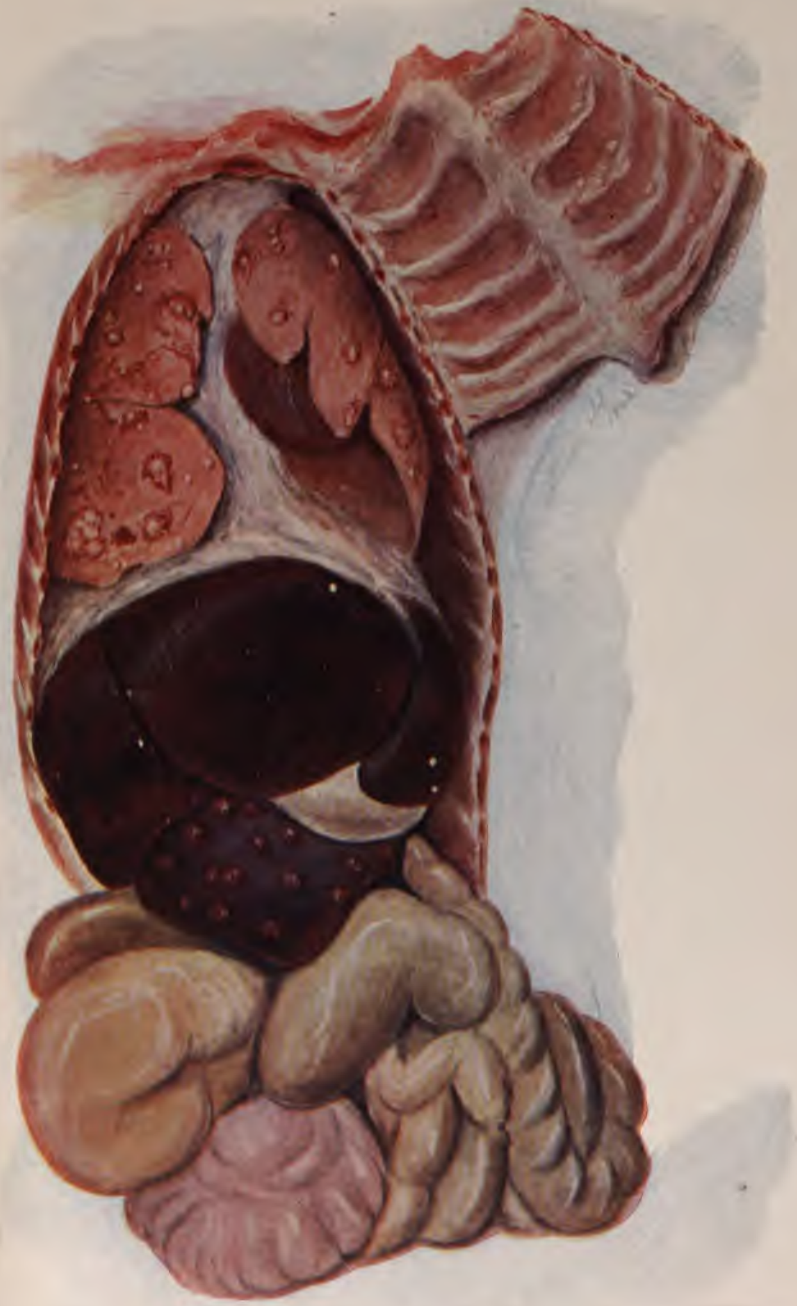
Tubercle bacilli in sections from Monkey No. 4. Bovi[illegible]s No. III.



Monkey No. 5. Rhesus.
Subcutaneous inoculation with pure culture human tuberculosis No. 50.



No. 6, Rhesus, subcutaneous inoculation with pure culture bovine tuberculosis



Monkey No. 7, Baboon. Fed on tuberculous milk. (Bovine tuberc

DISCUSSION OF MONKEY EXPERIMENTS.

The results obtained in the experiments with monkeys seem to justify the conclusion that no important difference exists between the two tubercle cultures used. One was a standard culture of human origin and the other a standard culture of bovine origin. An examination of the monkey records and of Plates XXV, XXVII, XXIX, XXX, and XXXI gives no other evidence against the identity of the two germs than that of a possible difference in virulence, and that a difference in virulence of tubercle bacilli from different sources exists, at times even when they are obtained from different organs of the same subject, is an old story.

As monkey No. 7 was kept under observation a long time, and gave no evidence of tuberculosis until a number of months had elapsed after she was fed milk actually containing tubercle bacilli, it may be well to say, in support of our conviction that the disease was due to the tubercle bacilli contained in the milk, that several other monkeys of the same species were kept under precisely similar general conditions, in other experiments, in adjoining cages in the same one-roomed house without contracting tuberculosis. This monkey indicates at one and the same time that tuberculosis contracted through ingestion progresses more slowly than tuberculosis induced by a subcutaneous injection; that a fairly generalized fatal tuberculosis can be produced by ingestion without specific lesions of the intestines; and, finally, that monkeys, notwithstanding their distance from cattle in the animal scale, are highly susceptible to the pathogenic properties of tubercle bacilli of bovine origin which gain entrance to their bodies with the food they eat. The question regarding the susceptibility of man to tubercle germs of bovine origin can not be more closely approached in an experimental way, and this experiment alone, supported by the large existing mass of circumstantial evidence of the infectiousness of tubercle bacilli of bovine origin for man, seems sufficient to warn every reasonable mind against the use of milk from tuberculous cows, and to point out with the greatest emphasis that it is desirable to take measures which will eventually eliminate all tuberculous cows from our dairy herds.

While it is not disputed that a majority of the persons who become infected with tuberculosis contract the disease from other human beings, it is maintained that cattle also constitute a very important source of infection. The importance of the latter source can not easily be overestimated in the light of the very considerable evidence which is accumulating in support of the view that human and bovine tuberculosis are not essentially dissimilar. It is true a difference does exist between certain tubercle bacilli of human origin and those of bovine origin, but it is not a specific difference or even a difference which permits the grouping of the germs as distinct varieties of the same species, but a difference practically confined to pathogenic virulence, and which forces us to regard the tubercle bacilli of bovine origin merely as more virulent than those of human origin.

REVIEW OF SOME OF THE MORE RECENT EXPERIMENTS CONCERNING THE INTERTRANSMISSIBILITY OF HUMAN AND BOVINE TUBERCULOSIS.

The well-known address of Prof. Robert Koch[1][a] before the British Congress on Tuberculosis in July, 1901, caused an enormous awakening of interest among medical men in all that concerned the relationship of human to bovine tubercle bacilli. In the paper referred to Koch expressed the belief that the infection of man with tuberculosis from bovine sources is of such rare occurrence that no preventive measures are necessary in this direction. He was led to this belief by the lack of direct evidence that such infection had taken place, and by the experiments conducted by himself and Schütz,[2] in which it was found that a number of tubercle cultures from human sputum would not infect cattle or certain other domesticated animals. This London address led medical investigators the world over to make experiments and observations bearing more or less directly on the intertransmissibility of human and bovine tuberculosis. By the fall of 1902 a large amount of evidence had been presented to show that certain tubercle bacilli of human origin are capable of causing a generalized tuberculosis in cattle, and many instances of the infection of men from cattle had been reported. These reports, which possibly modified Professor Koch's views in regard to the pathogenic power of human tubercle bacilli for cattle, did not influence his opinion in regard to the danger to human beings from the use of tuberculous meat and milk, as is shown in his latest paper[3] upon the subject. His views, as expressed in this paper, present the strongest possible statement of the position occupied by those who insist upon the noninfectiousness of bovine tuberculous virus for human beings. For that reason it seems desirable to quote in part the requirements which, in his opinion, should be met in order to establish the infectiousness of bovine tuberculosis for the human subject. The requirements are in part as follows:

> 1. Certain proof of tubercle in general and, where possible, the primary focus must be supplied. In adults we must, therefore, require the existence of unassailable clinical symptoms, and a necropsy when these are not present. In children the clinical symptoms are much too uncertain, and so a necropsy is always requisite with them.
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> 2. Other sources of infection must be excluded with certainty. The assurance that the person in question comes of a healthy family is under no circumstances sufficient. There

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[a] These figures refer to bibliography on page 98.

are numerous other possibilities of infection either inside or outside the family which come up for consideration. * * *

3. In each case of alleged infection from milk infected with perlsucht bacilli the condition of the rest of the people who have taken the same milk should be borne in mind. These fellow-consumers form to a certain extent a control experiment, and if of the numerous people who have drunk the suspected milk only a single one sickens, this weighs decidedly against the belief that this one person was infected by the common food. * * *

4. The source of the milk should be attended to. Since in recent years it has become more and more evident that milk containing tubercle bacilli is yielded only by cows affected with tuberculosis of the udders, the general statement that someone has drunk milk from a cow suffering from perlsucht no longer suffices to prove to us that perlsucht bacilli have really reached that person's organs of digestion. A man can certainly ingest milk from a cow suffering from perlsucht without coming into contact with perlsucht bacilli through it. It must be milk from a cow with tuberculosis of the udder, and therefore a statement relative to this point should not be lacking in a report on milk infection if it is to be considered complete.

It will be seen from the above statement that Doctor Koch requires absolute and direct proof of the infection of men with bovine tuberculous virus before he will recede from his position that there is practically no danger to human beings from tuberculous meat and milk. We are inclined to regard some of the conditions imposed by him as unnecessary and unreasonable because, owing to the insidious onset of this disease, and the fact generally admitted that tubercle bacilli which have entered the body may lie dormant for years without producing any evidence of their presence, it is impossible to say with absolute certainty when or where any given case of human tuberculosis had its origin. We are, therefore, forced to rely almost wholly upon indirect evidence as to the infectiousness of bovine tuberculosis for men. In our opinion the intertransmissibility of human and bovine tuberculosis is supported by so much indirect evidence of an overwhelming character that we are justified in regarding it as practically established. Absolute proof is greatly to be desired, but in its absence we must be governed by probabilities and base our regulations for the control of tuberculosis on them.

In the following pages are reviewed some of the most recent experiments bearing upon human and bovine tuberculosis, together with a portion of the literature concerning the transmission of tuberculosis to animals by feeding.

EXPERIMENTS WHERE INFECTION WAS BY MEANS OF DIGESTIVE TRACT.

Dobroklonski[4] has attempted to decide definitely the disputed questions whether tubercle bacilli can enter the body through the intestinal tract and whether a lesion of the intestinal mucous membrane is necessary for such infection to take place. The animals experimented upon were guinea pigs. The infecting material used consisted of tubercle cultures on glycerinized bouillon. A small glass tube with rounded ends was inserted into the throats of the guinea pigs and a few drops of a pure culture were allowed to flow through it. The animals were not fed for some little time after they received the culture and were guarded carefully against any outside infection. They were killed on the fourth, tenth, fifteenth, twentieth, twenty-fifth, thirty-second, and fortieth days, respectively, after being fed the culture. At the autopsy a careful macroscopic examination was made of the entire length of the intestine, and microscopic sections were made from large portions of that organ, those portions which indicated the slightest variation from the normal being given specially careful study. As a result of this extremely laborious experiment the author found that it is entirely possible for tubercle bacilli to pass through the normal intestinal mucosa of guinea pigs. He is not able to say just how the entrance is effected, but draws the following conclusions:

Tuberculosis may certainly infect animals through the digestive tract. For this infection to take place, no lesion of the intestinal wall is necessary; no epithelial desquamation; no local changes of any character; no previous inflammatory process. The tuberculous virus—the bacilli as well as the spores (sic)—can easily pass through the epithelial covering of the perfectly normal intestine. This penetration is particularly easy in cases where the contact of the tuberculous virus with the intestinal wall is prolonged, but for the penetration to take place it is not necessary for this contact to be prolonged. The tubercle bacilli as well as their spores (sic), if they are not long in contact with the intestinal wall, are not capable of provoking inflammatory processes or modifications of the epithelial lining of this wall. The tubercle bacilli probably have no definite way of gaining entrance into the organism—for example, by leucocytes exclusively—but they may be carried by the lymph current and later being arrested at some places in the tissues they there give rise to the formation of tubercles.

Nocard [5] says that in the case of cats, young animals are especially liable to contract tuberculosis through the digestive tract. He fed to four 6-weeks-old kittens and also to their mother a paste with which was mixed a very abundant culture of tubercle bacilli. All four kittens died within four months of a severe type of tuberculosis. The mother lived for a long time in good health, but when killed at the end of three years tuberculous lesions of the spleen, liver, and lung were found.

Clausen,[6] while holding the position of slaughterhouse inspector in the town of Husum, in Germany, was struck by the fact that the hogs slaughtered for the almshouse and hospital were more or less infected with tuberculosis. Hogs of the same breed fed in other places, however, were entirely sound. The tuberculous changes were usually found in the liver, mesenteric glands, cervical glands, or the lungs. Hogs suffering from generalized tuberculosis had to be condemned as unfit for human food. On this account it became very desirable to find the cause of this disease. As the hogs at the almshouse were supposed to be fed only upon barley, corn meal, cooked potatoes, and some green fodder, the food was not at first suspected. The stalls were in very good condition; nevertheless, before the introduction of fresh hogs they were cleansed with hot soda solution and disinfected with carbolic acid, and fresh lime was scattered over them. One day, quite accidentally, Clausen noticed that the refuse from the hospital portion of the institution, in which a number of tuberculous patients were being cared for, was thrown out to the hogs. He forbade the further continuance of this practice, and never found another tuberculous hog at that institution. As a result of this observation the author is convinced that hogs may contract tuberculosis directly from men. He consulted his day-book and found that hogs which had been cared for by men suffering with tuberculosis often showed that disease when slaughtered.

Tjaden[7] reviews the statistics concerning primary intestinal tuberculosis in children and also reports some experiments conducted by himself in collaboration with Hertel and Koske. They fed milk from tuberculous cows to sixteen young pigs. Only one of these developed a primary intestinal tuberculosis. The others had an infection of the mesenteric and also of the cervical lymph glands. From this fact the author infers that a great number of the cases of tuberculosis of the cervical glands in children may be caused by tuberculous milk, and that infection through the food is not always indicated by tuberculosis of the intestines.

Nocard[8] used six monkeys of the same origin for an experiment, which was briefly as follows: Three of the monkeys were reserved as checks. They remained perfectly healthy. The other three, which were fed several rations containing a small amount of a culture of bovine tubercle bacilli, became tuberculous after a short time. The localization of the lesions thus produced showed clearly that the intestinal mucous membrane was the entrance point of the virus, and there can be no doubt that the infection was the result of eating the infected food. The monkeys showed the same susceptibility to bovine tuberculosis that is seen in all other mammals; therefore, in Nocard's opinion, we have no right to suppose that there is a difference in the case of children. The milk from a cow suffering with udder tuberculosis must be considered as especially dangerous.

Cipollina[9] records the results obtained by feeding an ape with cow's milk, to which had been added a pure culture of bovine tubercle bacilli in the proportion of 1 öse to 150 c. c. of milk. This feeding was kept up for a month, the tubercle bacilli being administered every other day. Before the feeding commenced the animal was kept under observation for some time and carefully watched in order to see if it showed any signs of illness, and it was also tested with tuberculin before the experiment began, the test giving a negative result. The animal began to lose in weight and show symptoms of illness after a month and a half and died at the end of three months. The autopsy showed a severe tuberculosis of the abdominal organs and many nodules in the omentum and over the serous surface of the intestines. The mucous membrane of the stomach and intestine was not affected, with the exception of a few small areas in the colon, which were slightly hemorrhagic. This condition was due to the intestine being adherent to diseased mesenteric glands at those points. The kidneys and lungs exhibited many caseous nodules. This experiment, according to the author, shows, first, that the ape (Bertuccia) is susceptible to cattle tuberculosis by feeding; second, that the bovine tubercle bacillus may pass through the intestine without leaving any lesions at the point of entry.

Ravenel[10] has reported a very interesting experiment along the same line as those conducted by Dobroklonski, Tjaden, and Cippollina. Healthy dogs, after receiving a dose of castor oil, were fasted for twenty-four hours and then fed a single dose of melted butter and warm water containing a large number of tubercle bacilli. Three and one-half to four hours after feeding the dogs were killed and as much chyle as possible collected, together with the mesenteric glands. With this material guinea pigs were inoculated and microscopic examinations were also made. The entire intestine was carefully examined, but in no instance could a lesion be found. Of the ten dogs submitted to this treatment eight gave positive results. The author attributes the two failures to the fact that the tubercle bacillus used for feeding was very low in virulence, having been cultivated in the laboratory for a number of years. As a result of this experiment Ravenel concludes that—

> Under certain conditions tubercle bacilli pass through the normal intestinal wall with great facility and rapidity. The most favorable condition for this to take place appears to be during the digestion of food made up largely of fat. When we remember that the chyle is carried directly into the blood stream through the thoracic duct it is easy to understand how it is that infection through food may show itself first in the lungs, or at any rate that the lesion in the lung may be as old as the intestinal lesion. The claim that a food tuberculosis should show itself in a primary intestinal lesion is fallacious and misleading.

Schottelius[11] used three calves and two cows for a feeding experiment and reserved one cow and calf for control animals. The animals came from a mountainous region where tuberculosis did not exist. The calves were six weeks old and were sound and healthy. The infectious material was sputum from a tuberculous patient. The sputum was fed to the calves with milk and to the cow with green fodder. Each animal received about 50 grams at a feeding. From the 25th of May to the 29th of August 24 such feedings were given. There were no characteristic symptoms of illness. On the 20th of September the animals were slaughtered. Both control animals were perfectly healthy. The postmortem showed the following lesions in the three inoculated animals: In the cow, tuberculous enteritis, considerable swelling of the mesenteric glands, tuberculous caseation and calcification of the mediastinal and bronchial glands, and a caseous tuberculous pneumonia, with a few miliary tubercles on the pleura. In both calves there were greatly swollen, tuberculous, caseous, and calcified submaxillary glands and a few tuberculous mesenteric glands. The microscopic and bacteriologic examinations showed the presence of tubercle bacilli in the diseased parts.

Hüls[12] reports from his early practice the family of a miller, in which no case of tuberculosis had occurred until, within five years, seven members—six adults and a 13-year-old child—sickened and died of the affection. The beginning of the tuberculosis Hüls traces to the fact that a few years before the family became infected a strange cow, suffering with tuberculosis, was purchased, and the miller's entire herd of cows became infected through the entrance of this new animal. The incident is recognized by the author as not proving the identity of human and bovine tuberculosis, but, taken together with other observations, points strongly to the possibility of their intercommunicability.

Heller[13] agrees with Koch that hereditary tuberculosis does occur, but is so rare that it can be left out of practical consideration. He disagrees with Koch as to the infectiousness of bovine tuberculosis for man, and concludes from the examination of a large amount of material that primary infection of the intestinal tract occurs with a considerable degree of frequency. This investigator recognized how difficult it is to obtain data regarding the original center of disease by the examination of tuberculous cadavers because of the advanced character of the lesions and therefore used the material from diphtheria autopsies, as it is well known that tuberculosis frequently follows diphtheria. Among the 714 autopsies made, 140, or 19.6 per cent, showed the presence of tuberculosis. Of the latter, 43, a small fraction less than 31 per cent, showed primary tuberculosis of the intestinal lymph glands, and 10 additional cases showed disease of the abdominal organs associated with lung affection.

In the presence of abdominal tuberculosis in children the food must be suspected, and of this cow's milk is the most important. The objection that children lie on the floor a great deal and put all manner of things into their mouths, and contract intestinal tuberculosis in this way, does not explain why children rarely suffer from pulmonary tuberculosis, to which they are equally exposed by their habit of crawling, which facilitates the breathing of dust charged with tubercle bacilli.

Heller shows the infectiousness of bovine tuberculosis for man in a very striking and well-investigated case, in which a man who pricked milk into his skin in order to remove tattoo marks developed lupus at the point of inoculation. On the ground of these investigations Heller strongly opposes a relaxation of the former regulations for the control of bovine tuberculosis.

INOCULATION EXPERIMENTS.

Cipollina[9] describes the inoculation of a calf with a culture of human tuberculosis; details not given. The inoculation was made in the following manner: The animal was allowed to inhale tubercle bacilli through an opening in the trachea, and also received an intraperitoneal injection of 10 c. c. of the same culture. After twenty days the animal was well and was inoculated for the second time intraperitoneally with 20 c. c. of the same culture. The animal died after two months, but showed no signs of tuberculosis. The author concludes that cattle are very resistant to human bacilli, but in the light of researches upon ordinary experimental animals he believes that the human bacillus may infect all animals that are susceptible to the bovine bacillus, the only difference being that the latter is almost always more virulent than the former. This explains why cattle can resist human tuberculosis and succumb to bovine tuberculosis, and what is true of other animals is probably also true of man. The bacillus of bovine tuberculosis is, therefore, more virulent for man than the human bacillus itself.

Bang[14] noted the following in regard to his experiments upon the transmission of human tuberculosis to cattle. In two instances human tuberculosis was inoculated into the anterior chamber of the eye of calves with positive results. In the first case the material was taken from a tuberculous human lung. A guinea pig was inoculated with this material and the spleen of this guinea pig furnished material for the inoculation in both eyes of an 8-weeks-old calf. The primary inflammation was unimportant and quickly disappeared, but about eighteen days later a severe tuberculous iritis and conjunctivitis developed. After about seven weeks the calf was killed. At the autopsy both eyes showed a distinct tuberculous iritis. The other organs of the body, however, exhibited no changes. In the second case Bang injected into the anterior chamber of the eye of an 8-weeks-old calf some pus which was obtained from the tuberculous lymph gland of a child. The result was quite similar to that in the first case. The pus was quickly absorbed and a week after the inoculation the eye was apparently in a normal condition. Three weeks after the inoculation a tuberculous iritis developed and was followed by a keratitis and a conjunctivitis. Four and one-half months after the inoculation the iris was studded with white nodules.

Both of these cases show that human tuberculosis is communicable to cattle. They indicate also, however, that human tuberculosis pursues a slower and more benign course in cattle than the true bovine tuberculosis.

Orth[15] reports the following experiments: Three calves, three hogs, and three goats were used. The animals were all obtained from yards which were known to be free from infection, and the calves gave a negative reaction to the tuberculin test shortly before the commencement of the experiments. The infectious material was obtained from a case of phthisis cavernosa by inoculating a guinea pig and then obtaining cultures from this animal upon brain and other media. In the experiments bouillon cultures of the organisms were used and in some cases tuberculous organs from rabbits which had been injected with such cultures.

Of the three calves, the first one, which received a bouillon culture, injected into the lung through the trachea, gave an entirely negative result. The second, which was inoculated between the abdominal muscles with a suspension of the pure culture, showed only a local caseous abscess. Both animals were killed five and one-half months after the beginning of the experiment. The third calf, which was inoculated in the peritoneal cavity with two pieces of tuberculous kidney from a rabbit, died on the twenty-sixth day of a general tuberculous peritonitis. The serous membranes were covered with miliary and submiliary tubercles. The great omentum, which was adherent to the peritoneum, was sprinkled throughout with nodules. Small nodules were visible on the serous membrane of the intestines. The mesenteric, portal, and cardiac lymph glands were much enlarged and showed grayish-white nodules upon section. The retrosternal lymph glands were much enlarged and congested, and small nodules were visible upon section. The left shoulder gland and other lymph glands were swollen and some exhibited tuberculous changes. The other organs were free from tuberculosis. The microscopic examination of the peritoneal nodules and the various lymph glands, especially the retrosternal and submaxillary glands, showed typical tuberculous granulations containing giant cells and many tubercle bacilli, which were especially abundant in the giant cells.

The guinea pig inoculated from this calf died within a few days, so that this experiment could not be carried further. It can be said, however, that human tuberculosis has been communicated to a calf, and not simply a local disease, but a progressive, fatal tuberculosis was produced. There can be no doubt that this calf was infected with human tuberculosis, for in the author's various experimental animals no case of spontaneous tuberculosis had developed and no bovine inoculations had been made. The condition of the calf could not be ascribed to the action of dead bacilli, for the bacilli with which the calf was inoculated were inclosed in a tuberculous kidney tissue and must have spread over the entire peritoneum and also to portions of the body far removed from the point of inoculation.

In the case of the three hogs, the two which were inoculated intraperitoneally with the bouillon culture gave practically negative results. The third hog was inoculated through the trachea into the lungs with a bouillon culture. After five and one-half months the animal was killed. In the thymus gland and in the membranes around it there were many yellowish tuberculous nodules. The left lung was free from tuberculosis, but in the inferior lobe of the right lung there were found a large number of submiliary and miliary tubercles. No other tuberculous changes were found. The microscopic examination of the nodules presented a typical picture of tuberculous granulations containing giant cells and exhibiting a central caseation. Tubercle bacilli were present.

The three goats all showed tuberculosis following inoculation, though it is worthy of note that the two most marked cases resulted from inoculation with the tuberculous organs of a rabbit. The first animal, which was inoculated with a bouillon culture through the trachea into the lung, showed a number of subcutaneous nodules near the point of inoculation, a large caseous nodule in the thymus gland and a number of yellowish gray nodules in the inferior lobes of the right and left lungs. No lesions were found in the abdominal viscera except a few yellowish nodules in the liver, which, upon microscopic examination, were found to be tuberculous in character.

The second goat was inoculated intraperitoneally with a small piece of lung from a tuberculous rabbit. The animal was killed after five months and showed the following lesions: A number of nodules in the muscles and subcutaneous tissue at the point of inoculation. A number of small grayish, translucent nodules were found scattered through the omentum. They were found especially in the portion near the stomach and some of them hung by small pedicles resembling polypi. Similar changes were found in smaller number on the diaphragm and in the neighborhood of the lymph glands surrounding the heart. On the pleural surface of the diaphragm these nodules occurred singly. On the anterior border of the liver near the gall bladder there was found a nodule about the size of a pea. Microscopic examination showed the nodules to be tuberculous granulations containing giant cells with a necrotic center and often lime salts were present. Bacilli were found, although in small numbers.

The greatest changes were found in the third goat, which was inoculated with the same tuberculous kidney with which calf No. 3 was inoculated. A fragment about the size of a bean was introduced into the peritoneal cavity of the goat. The animal was killed at the end of five and one-half months. A number of tubercles were found around the point of inoculation. There was a large group of caseous nodules on the adjoining surface of the stomach, numerous caseous nodules in the omentum, many of these latter having small pedicles. There were some nodules and granulation tissue attached to the capsule of the liver. The interior of this organ, however, was free from tuberculosis. The retroperitoneal lymph glands were very large but not caseous. All other organs appeared to be normal. Nodules from the various diseased areas were examined microscopically and showed tuberculous new formations with giant cells, central necrosis, and calcification. Tubercle bacilli were easily demonstrated. There can be no doubt as to the tuberculous character of the lesions described nor that they were produced by human tubercle bacilli. Therefore the author takes issue with Koch's statement that tuberculosis of man can not be communicated to cattle.

To answer the question as to whether he has really obtained a perlsucht or simply a tuberculosis different from that of cattle, the author points out that in the third goat the abdominal lesions were entirely of the perlsucht character. He also points to the case reported by Baumgarten in which by injection of perlsucht bacilli into cattle, a generalized miliary tuberculosis was produced without any resemblance to the typical perlsucht. The morphological changes can not be relied upon to differentiate between human and bovine tuberculosis, because these changes depend upon the condition of the animal as well as upon the organism itself. How little the perlsucht form of a tuberculous disease is dependent upon the perlsucht bacillus has been shown by Troje and Tangl who, by subjecting human tubercle bacilli to the vapor of iodoform, succeeded in producing a typical perlsucht in rabbits.

Orth concludes that it is proven that human tuberculosis can be communicated to cattle. It must be remembered also that the danger of the communication of bovine tuberculosis depends not only upon the transmission of bovine bacilli, but also upon the constitution of the person who is exposed to them.

Fibiger and Jensen[16] report the results of their experiments with human tuberculous material obtained from the various hospitals of Copenhagen. They report in all five cases of tuberculosis in the following subjects: (1) 42-year-old woman, (2) 11-year-old girl, (3) 6-year-old boy, (4) 19-months-old girl, and (5) 4-months-old boy. In all of these cases the infection appears to have begun in the intestines and in some the disease was practically confined to the abdominal organs.

(1) A 3-months-old calf was inoculated in the thoracic cavity with a suspension made from a mesenteric gland of case No. 1. This calf

remained apparently in good condition and was killed at the end of six months. Two miliary tubercles were found on the pleura and a few fresh pearl nodules were found on the pulmonary pleura; otherwise the animal was in good health.

(2) A 3-months-old calf which had been subjected to the tuberculin test was inoculated intraperitoneally with a suspension made from the spleen of a guinea pig which had been inoculated with a mesenteric gland from case No. 2. The health of the calf was not visibly affected by the inoculation. It was killed at the end of the fifth month. In the omentum was found a large number of small red growths and about twenty small, fresh, pearl nodules. On the diaphragm, also, there were some small nodules and excrescences; on the pulmonary pleura a few excrescences.

(3) A calf 2 to 3 months old which had withstood the tuberculin test was inoculated intraperitoneally with a suspension made from the spleen of a guinea pig which had been inoculated from case No. 3. There were no acute symptoms following the inoculation, although at the end of three weeks and later there was a slight rise in temperature. The calf was killed about the end of the fifth month. The omentum was filled with tuberculous new growths and showed countless small nodules of varying size. All lesions were recent; a few showed traces of caseation. There were some small nodules found on other portions of the peritoneum. The surface of the spleen and liver was covered with small pearl nodules, as was the diaphragm. Some of the mesenteric glands were enlarged. In the lungs a few small areas of atalectasis; no tuberculosis. The bronchial and posterior mediastinal glands were enlarged but showed no caseation.

(4) A calf 2 to 3 months old which had been subjected to the tuberculin test was inoculated subcutaneously on the right side of the neck with a suspension made from the mesenteric gland of case No. 3. The animal showed no very marked symptoms following the inoculation and was killed at the end of the seventh month. There was a large caseous mass at point of inoculation. The neighboring glands were enlarged, caseous, and calcified. The lungs had scattered through them many small miliary nodules and there were a number of excrescences attached to the pulmonary pleura. No caseation in these excrescences. The bronchial and posterior mediastinal glands were enlarged, hard, and dotted with fresh caseous and calcified nodules. The liver and spleen had scattered through them miliary tubercles. The omentum was filled with fine, diffused, red, new growths. In the mesenteric glands there was no evidence of tuberculosis.

(5) Two 10-days-old calves were inoculated subcutaneously on the side of the neck with a suspension made from a mesenteric gland

from case No. 5. Both of these animals died within three weeks of the inoculation and evidently from secondary infection. Although the calves died so soon there developed, nevertheless, a considerable local tuberculosis rich in bacilli

From calf No. 2, case 5, a third calf was inoculated and from calf No. 1 an old cow was inoculated. Calf No. 3, inoculated from calf No. 2, was fourteen days old and was injected subcutaneously in the right side of the neck. A large abscess formed at the point of injection. At the end of about two months the calf, being in a dying condition, was killed. The autopsy showed, in addition to the local lesions, tuberculosis of the adjacent lymph glands. There were many new growths on the costal and pulmonary pleura and also on the pulmonary surface of the diaphragm. The lungs contained a countless number of minute nodules, some of which were as large as hemp seed. The bronchial and mediastinal glands were enlarged and caseous. The liver, spleen, and kidneys had miliary tubercles scattered through them. The intestinal wall was very rich in fresh nodules and small superficial ulcerations. The mesenteric glands were enlarged and tuberculous. The omentum was rich in small new growths.

A cow about 10 years old, inoculated on the left side of the neck with material from calf No. 1, developed a phlegmonous abscess at the point of inoculation which was accompanied by fever, and tubercle bacilli were found in the pus. At the end of four months the cow was killed. In addition to the local abscess the neighboring glands were enlarged, caseous, and calcified. Miliary tubercles were scattered through the lungs. In the posterior mediastinal gland a nodule was found the size of a pea; in the liver, a small number of miliary tubercles. The other organs were normal.

Thus, in three cases of tuberculosis in children the bacilli present were virulent, some of them in the highest degree, for calves, and it is probable that the disease in the children was caused by bacilli which came from cattle. In the five cases the greatest variation in virulence for calves was found, ranging from nothing to the highest degree, and it is especially noteworthy that the virulence of these bacilli seemed to decrease as the age of the patient increased. Koch claimed that one could distinguish between human and bovine tuberculosis by inoculating calves subcutaneously. If this is true, then three of the cases above cited must be considered as perlsucht, and the assertion that tuberculosis of cattle is not virulent for men is disproved.

Karliński[17] succeeded in communicating tuberculosis to cattle by means of human tuberculous virus ten times in twenty-three attempts. The mode of inoculation varied. Some of the animals were inoculated intraperitoneally, some intrapleurally, some intratracheally, some into the udder, and some subcutaneously. He compared the cultures of human and bovine tubercle bacilli, but found absolutely no difference between them, either microscopically or macroscopically, except in the rapidity of growth. He considers that the chief difference is the greater resistance of cattle to human than to bovine bacilli. He has attempted to increase the virulence of the human tubercle bacillus by passing it through calves. With this object in view he inoculated one calf subcutaneously and intraperitoneally at the same time. At the end of two months the animal showed a distinct tuberculin reaction and was killed, and tuberculous changes were found in the mesenteric glands, liver, and spleen; some of the lesions showed a caseous degeneration. He recovered a culture from this animal and inoculated a second calf. This calf showed a tuberculin reaction in less than a month, but was allowed to live until the end of two months, when it was killed and showed a much more generalized tuberculosis than was found in the first animal, thus indicating that this particular tubercle culture had been increased in virulence by its passage through a calf.

Thomassen,[18] in the spring of 1899, tested two calves, aged 8 and 4 weeks, with tuberculin, obtaining negative results. The milk with which these animals were fed was taken from a cow which did not react to tuberculin. The 8-weeks-old calf received intraabdominally a culture upon glycerinized potato which was derived from the cerebral exudate of a child affected with tubercular meningitis. The animal remained well and was tested with tuberculin after two months and gave a good reaction. When the animal was killed, however, one month later, notwithstanding a most careful postmortem examination, no trace of tuberculosis was found. The calf 4 weeks old was inoculated in the anterior chamber of the eye with a culture of tuberculosis upon glycerinized potato which was derived from a case of tuberculous arthritis. After about a month this animal was tested with tuberculin, but failed to react. It was killed a short time afterwards and found to be affected with a generalized tuberculosis. The progress of the infection from the eye to the lungs was easily traced through the chain of lymphatic glands.

Some months later a cow about 2 years old, in perfect health, was tested with tuberculin and did not react. Shortly afterwards this animal was injected in the trachea with a culture of tuberculosis grown upon potato. This culture was obtained from a case of human renal tuberculosis. After two months a tuberculin injection failed to produce reaction. A few days after this second tuberculin test a culture was injected into the thorax and into the abdominal cavity. In making the abdominal injection some of the material was deposited in the muscular tissue. As a result of this an abscess containing purulent material formed and was found to contain tubercle bacilli. After five months the animal was tested with tuberculin without reaction. About ten months after this the animal was killed and showed not the slightest trace of tuberculosis. A fourth cow, 2 years old, was tested with tuberculin without reaction, and a culture of tuberculosis obtained from a case of renal disease in a man was injected into the anterior chamber of the eye. This animal after two months gave a marked tuberculin reaction, and was in very bad health. Six months after the inoculation the animal was killed. There were tuberculous lesions in the eye and in one bronchial gland, but unfortunately a histological examination could not be made. Thomassen's experiments show that it is difficult, but not impossible, to produce tuberculosis in cattle by means of cultures of the human bacillus. He thinks the much greater virulence of the bovine bacillus, which is generally admitted, should urge, contrary to the advice of Koch, a most rigid inspection of all meat and milk.

Arloing[19] inoculated thirty-three animals of various species with bacilli of human origin. The results were positive in every instance. Five separate cultures of human tuberculosis were used, cattle, sheep, goats, donkeys, and hogs were infected by intravenous injections and exhibited tuberculous lesions of different degrees. The human cultures varied greatly in virulence, but microscopic examination demonstrated that even the weakest had produced true tuberculous lesions. Compared with injections of bovine virus it can be said that, as a rule, the bovine virus is more virulent than the human, as all of the animals inoculated with bovine tuberculosis died within forty-four days, at the most, and the majority of those inoculated with human bacilli were killed. Arloing concludes:

> (1) Human tuberculosis is infectious for cattle, and at times, by certain methods of inoculation, it brings about lesions having the character of bovine tuberculosis.
>
> (2) The human bacillus is not always of the same virulence and does not show the same degree of activity toward different species of herbivora.
>
> (3) In some cases human bacilli are as virulent as germs of bovine origin. In other instances, on the contrary, the virulence is so reduced that it appears to be nil, especially for the bovine species.
>
> (4) Human bacilli of attenuated virulence always produce in the lung at least, following intravenous injections, lesions which are visible with the microscope.
>
> (5) The variations in the virulence of the bacillus account for the apparent negative results which have led Messrs. Koch and Schütz to believe in the duality of species. The unity of human and bovine tuberculosis should be maintained, and prophylactic measures which arise therefrom should be continued, especially with regard to the use of milk.

Ravenel[20] describes two cultures of the tubercle bacillus obtained from the mesenteric glands of two children. One (culture B B) he found to be quite as virulent for calves upon intravenous inoculation as the bovine bacillus, and the other (culture U) had a virulence decidedly above that of the ordinary human cultures. Culture

B B corresponded morphologically and culturally more nearly to the bovine type than to the human. He also reports the results of another experiment made by Dr. Leonard Pearson, in which a calf received large amounts (925 c. c. in all) of a human tubercle culture of moderate virulence at intervals extending over a period of four months, in the form of subcutaneous, intravenous, intrapulmonary, and intraperitoneal injections. This culture after successive passages through calves, showed a great increase in virulence.

Stenström[21] records experiments upon calves of reaction-free cows which were raised on boiled milk. Eight of these calves were inoculated in various ways with tuberculous sputum which was rich in tubercle bacilli. Three of the calves died shortly after inoculation and were left out of count. The remaining five were slaughtered six months after inoculation, and the autopsies showed the following results: Calf No. 820, inoculated into the lung, showed many tuberculous adhesions upon the costal and diaphragmatic pleura, as well as tuberculous areas in the mediastinal glands. Calf No. 833, infected by intratracheal injections, showed partly calcified areas in the anterior and posterior mediastinal glands and in the bronchial glands. Calf No. 224, inoculated intraperitoneally, showed many calcified areas in the omentum and enlargements of the glands within it, a fibrous exudate on the serous membrane of the peritoneal cavity, many tuberculous areas in the liver the size of a pinhead, and some adhesions on the surface of the right lung. Calf No. 94 had pulverized sputum sprayed into the nose and showed only slight inflammation of the pulmonary pleura. Calf No. 818, inoculated subcutaneously, showed only a large abscess at the point of injection and a proliferation of tissue around this abscess.

These results differ from those of Koch. None of Koch's nineteen calves showed any tuberculosis of the internal organs after six or eight months; only a small pus area containing a few tubercle bacilli was found. Stenström found in his animals that the tuberculosis spread from the point of infection to the internal organs and lymph glands, and also to the serous membranes. Indeed, in No. 224 tuberculous areas were found in the liver. Koch's assertion that human tuberculosis is different from bovine tuberculosis, and that human tuberculosis can not be communicated to cattle is opposed by this investigator, who found it quite easy to infect cattle with human tuberculosis, although he recognizes that human tubercle bacilli are relatively less virulent for cattle than bovine bacilli. He believes if his animals had been allowed to live longer, and had been subjected to unfavorable conditions such as illness, and so forth, the disease would possibly have been more advanced. In other words, a generalized tuberculosis is not necessary to prove that infection has taken place, as it is well known that bovine tuberculosis can remain local for many years, and at the autopsy only a few small tuberculous areas in the lymph glands are found.

Nocard[22] has been able by the use of collodion sacs containing human or bovine tubercle cultures introduced into the peritoneal cavity of fowls to transform these mammalian tubercle bacilli into cultures which have the morphological and cultural characteristics of avian tubercle bacilli and which possess a virulence for fowls equal to that of the avian tubercle bacillus, but their virulence for guinea pigs was apparently lost.

Svensson[23] attempted to infect healthy calves with tuberculous sputum by means of subcutaneous intratracheal, intraperitoneal, and intrapulmonary injections or through the inhalation of pulverized sputum. About six months after the beginning of the experiment the animals were killed, and the autopsies showed that the serous membranes, as well as the lymph glands in the neighborhood of the inoculations, were tuberculous. In the opinion of the author his experiments show that the human tubercle bacillus possesses relatively slight virulence for cattle.

Dean and Todd[24] made some experiments, the object of which was to ascertain whether the human tubercle bacillus undergoes any marked change in virulence for cattle by passage through the pig, cat, rat, rabbit, or mouse. The authors give an account of their experiments in detail and reach the following general conclusions:

(1) That the hog is capable of contracting a rapidly fatal generalized tuberculosis as the result of infection with the human bacillus.

(2) That the human tubercle bacillus is not markedly increased in virulence for the calf by a single passage through the pig, cat, rat, or rabbit.

(3) That the human tubercle bacillus is by no means innocuous to the calf, as the control animal injected directly with sputum contracted an extensive glandular tuberculosis.

The authors used tuberculous sputum for all of their inoculations instead of pure culture. They noted that sometimes the first animals in a series died earlier than those inoculated later with tissue from the first animal. They explain this by calling attention to the fact that in the case of the second inoculation the tubercle bacillus was present almost always alone, whereas in the sputum inoculations at the beginning of the series many other bacteria were associated with the tubercle bacillus, and the earlier death of the first animals in some cases is to be attributed to the action of the associated organisms rather than to a more exalted virulence of the tubercle bacillus.

De Jong[25] describes, in the latter part of his paper, experiments which he made with a bacillus of human origin, which is very virulent for cattle. The material was obtained from a peasant woman 27 years of age, without hereditary taint, whose occupation brought her in frequent contact with animals. This woman was affected with pulmonary tuberculosis and a guinea pig inoculated with some of her sputum became tuberculous. Cultures from the spleen of this guinea pig served for the two following experiments:

A calf 6 weeks old, weighing 65 kilograms, received in the jugular vein 6 c. c. of an emulsion of culture. The animal had not reacted to tuberculin. Five days after the injection the temperature exceeded 40° C., and it remained elevated until death, which took place at the end of nineteen days. The weight had fallen to 53 kilograms. The autopsy showed extensive tuberculous lesions of the lungs, liver, spleen, kidneys, and lymphatic glands. On the pleura were found alterations characteristic of the early stages of pearl disease.

A goat which was likewise perfectly healthy, weighing 17 kilograms, was inoculated in the jugular vein with 5 c. c. of the same emulsion. This animal died in twelve days of a generalized tuberculosis.

Two other inoculation experiments with this same bacillus are also reported. One was an intrapulmonary injection of a calf and was followed by a generalized tuberculosis. The other was a subcutaneous inoculation of a calf with the same culture, death taking place at the end of fifty-six days. The weight had fallen from 58 kilograms at the beginning of the experiment to 53 kilograms at the time of death. The autopsy revealed very severe generalized tuberculosis, involving the lungs, liver, spleen, kidneys, and lymphatic glands.

It can not be denied that the above case of human tuberculosis is an instance of infection by the bovine bacillus, or by a human bacillus which possessed equal virulence with the bovine bacillus for cattle. Either one of these hypotheses contradicts the theory put forth by Koch.

Wolff[26] mentions a case of primary human intestinal tuberculosis, the virus from which produced generalized tuberculosis in a calf. This case was previously reported in the Deutsche Med. Wochenschrift, 1902, No. 32, where all the details are given of the care which was taken in the inoculation of the virus into a tuberculosis-free calf (tested with tuberculin); also of the clinical course of the disease which followed the subcutaneous injection into the neck, the fact that the animal twice gave an exquisite tuberculin reaction at four and eleven weeks after injection, and, finally, the autopsy upon the calf and the microscopic examination eighty-three days after the beginning of the experiment. The autopsy showed the greatest alterations at the point of inoculation, and in the inner organs changes that are typical of perlsucht. Briefly, the autopsy record is as follows: At the point of inoculation in the neck were found the oldest lesions. A tumor about the size of a child's head with a central cavity which contained a caseous pus, the cavity surrounded by a thick granulation membrane and sprinkled with calcareous deposits. In the neighborhood of the cavity were several glands the size of a small apple, with numerous caseous and calcareous nodules. In the neighborhood of the point of injection the shoulder glands and the pharyngeal glands were greatly swollen with caseous and calcified nodules. The pleura, pericardium, omentum, and the capsules of the spleen and liver were covered with characteristic tumors which varied in size from a millet seed to lentil, bean, and cherry sized nodules. In addition, tumors were found on the serous membranes and in the lung tissue. In the pulp of the spleen, and in the parenchyma of the liver and kidneys, miliary nodules were visible. The microscopic examination of these nodules frequently showed typical epitheliod-celled tubercles, together with giant and round cells, their structure being very similar to the human tubercle. Tubercle bacilli were found in the nodules of all the organs. Upon section and examination of the microscopic preparations, caseation and calcification of the tuberculous new growths at the point of injection and the neighboring glands were found, while the nodules in all distant organs (pleura, pericardium, lung, omentum, liver, spleen, and kidneys) were still fresh and showed neither caseation nor calcification. This microscopic evidence in connection with the identical macroscopic appearance, namely, the fact that the calcification and caseation were found only at the point of injection and in the neighboring glands, and, further, the clinical symptoms which were observed, indicate with certainty that the tuberculous process began first of all at the point of injection and spread from there, producing a general infection of the organism. Taking everything into consideration, there can be no doubt that here is a case of virulent perlsucht in a calf, which was brought about by the inoculation of material from a case of primary intestinal tuberculosis in man. According to Koch, such an inoculation of a calf with tuberculous material from such a case of primary intestinal tuberculosis will enable us to determine positively whether the infection was of human or bovine origin.

The author concludes his paper with a general discussion of the tuberculosis question, and takes the position that even if all the experimental proof of the identity of human and bovine tuberculosis is faulty, we should still, so long as there is any doubt about the transmissibility of bovine tuberculosis to man, take precautions to prevent possible infection.

Theobald Smith[27], in a recent communication to the Association of

American Physicians, described a culture of tuberculosis, isolated from the mesenteric gland of a child, which corresponded morphologically and culturally quite closely to the bovine bacilli with which it was compared. A steer inoculated intrathoracically with this culture became quite ill and was killed thirty-eight days after the inoculation. The autopsy and subsequent microscopic examination revealed tuberculosis of the lungs, mediastinal lymph glands, the liver, and the spleen. The pathogenic power of the culture appeared to be slightly below that of the ordinary bovine tubercle bacillus, but it undoubtedly possessed the ability to produce a genuine tuberculosis in the inoculated steer. Doctor Smith is of the opinion that this organism, on account of its cultural characters, its morphology, and its pathogenic power, should be considered as a bovine bacillus, and that the child from whom the culture was obtained was probably infected directly from cattle through milk.

Park[28] fed tuberculous sputum to four nonreacting calves and at the same time inoculated them subcutaneously with similar sputum. A fifth calf served as a control. After two and one-half months three of the calves reacted to tuberculin. At the autopsy one of them showed a few enlarged lymph glands, but without tubercles. The others had gained in weight. The tuberculin reaction in these cases Park attributes to the abscess at the seat of inoculation.

Mursajew[29] conducted a number of experiments to determine the relation between human and avian tuberculosis. He isolated a number of avian cultures and inoculated guinea pigs, rabbits, and pigeons with both varieties. He found that pigeons are generally fairly resistent to avian tuberculosis and says that their susceptibility to human tuberculosis is not very great, although their susceptibility to both organisms is influenced considerably by starvation. A passage of human tubercle bacilli through the pigeon's body does not increase their virulence for pigeons. Guinea pigs are quite susceptible to both forms of tuberculosis. There are certain slight differences in the pathological changes produced by the two strains of tubercle bacilli, but they are slight and amount to very little. Of five rabbits the author succeeded in infecting two with avian tuberculosis. He does not believe that the virulence of tubercle bacilli is increased by their passage through the bodies of animals.

Karlinski[30] reports fourteen attempts to communicate tuberculosis to cattle. The human cultures were all derived from sputum. Cattle were inoculated by different methods, some intravenously, some intraperitoneally, some subcutaneously. Certain cattle were inoculated with the human bacillus cultivated directly upon Hesse's medium without passage through the animal body. Others were inoculated with the same cultures which had been passed through several guinea pigs. In certain instances the human virus was transferred from one calf to another in order to determine the effect of such passages upon the virulence of the human bacillus. Certain of the animal cultures were grown upon beef serum which was derived from an animal which had been previously inoculated with human tuberculosis. The author considers that thirteen out of fourteen experiments were successful in communicating human tuberculosis to cattle; also that the virulence of the tubercle bacilli was sensibly increased by passage through guinea pigs, and that human tubercle bacilli which have passed through cattle are markedly increased in virulence for cattle. As a result of these experiments Karlinski states that it is possible to communicate human tuberculosis to the usually resistant Bosnian cattle; that the disease affects primarily the lymph system, but a generalized tuberculosis may be produced by certain means, such as increase of virulence by passage through guinea pigs or cattle, and by intravenous inoculations. In his opinion no distinction should be made between human and bovine tuberculosis.

Fibiger and Jensen[31] quite recently reported experiments with 5 additional human tuberculosis cultures. These cultures were obtained from: (1) A man 92 years old, who died of primary intestinal tuberculosis; (2) a girl 12 years old, who died of a generalized tuberculosis which apparently originated in the intestine; (3) a girl 7 years old, who died of a tuberculosis which had its origin in the intestine; (4) a man 40 years old, who died of an intestinal tuberculosis; (5) a child 3½ years old, who died of a generalized miliary tuberculosis.

Material taken from case No. 1 was apparently completely lacking in virulence for a calf when inoculated subcutaneously. A calf inoculated subcutaneously with material taken from a mesenteric gland of case No. 2 developed a tuberculosis of the shoulder gland and of the inferior glands of the neck. This culture evidently possessed little virulence for cattle. The spleen of a guinea pig which had been inoculated with a portion of a mesenteric gland of case No. 3 caused a generalized tuberculosis in a calf on subcutaneous inoculation. Material from a mesenteric gland from case No. 4 produced generalized miliary tuberculosis in a calf on subcutaneous inoculation. A portion of the liver of a guinea pig which contracted tuberculosis as the result of inoculation with material from case No. 5 was used for the subcutaneous inoculation of a calf in which it produced a localized tuberculosis associated with enlargement, caseation, and calcification of the shoulder and of the neck glands on the side of inoculation.

Among the ten cases quoted by Fibiger and Jensen in their two papers, we find that of the four adults from whom material was obtained one furnished a virus which was capable of causing a generalized tuberculosis in cattle. The other three were either entirely lacking in virulence or of only very weak virulence for cattle. Of the six children, four furnished tubercle bacilli of great virulence and two furnished bacilli of low virulence for cattle. Eight of the cases of human tuberculosis were apparently due to a primary intestinal infection. Out of five cases of primary intestinal tuberculosis in children, four furnished bacilli which were of marked virulence for cattle.

The German Commission, headed by Kossel[32], which was appointed to inquire into the various questions raised by Koch in his London paper, reported the isolation of thirty-nine cultures from various cases of human tuberculosis. Nineteen of these cultures produced no lesions in cattle after subcutaneous inoculation; nine cultures produced very slight tuberculous changes in the prescapular gland adjacent to the point of inoculation; seven cultures caused a more marked affection of the prescapular glands, but the disease did not spread to other portions of the lymphatic system; and the remaining four cultures of human origin caused a generalized tuberculosis in the calves which were inoculated subcutaneously with them. It will be seen, therefore, that four of the human tuberculosis cultures, or slightly more than 10 per cent, produced generalized tuberculosis in cattle, and it is very significant that these four most virulent cultures were all obtained from children, who, it is generally admitted, are in more danger of exposure to bovine tuberculosis through food than adults who consume proportionately very much less milk.

COMBINED FEEDING AND INOCULATION EXPERIMENTS.

De Haan[33], after a few subcutaneous and intravenous inoculations of goats, cattle, monkeys, and a horse, and after some feeding experiments with monkeys, a pure culture of human tuberculosis from sputum being used in all cases, formulates the following conclusions:

(1) It is possible to bring about in Javanese goats, cattle, and horses, by inoculation with human tubercle bacilli from sputum, certain pathological changes in the tissues which, macroscopically as well as microscopically, agree perfectly with the lesions found in Europe in animals which have been infected in a natural manner. The animals which showed these changes were not in the best of health at the time of inoculation. Perfectly healthy sheep and cattle were able to resist infection with the tuberculous material.

(2) There does not exist in the above-named animals a race immunity from tuberculosis. The absence of this disease among the animals of Java must be ascribed to other causes.

(3) The monkey is quite susceptible to infection with tubercle bacilli of human origin.

(4) The feeding of material containing tubercle bacilli can give rise to a tuberculosis of the lungs and of the bronchial lymph glands, together with—

(a) A tuberculosis of the mesenteric lymph glands without perceptible change in the intestines;

(b) Without any other localization of the tuberculous process.

(5) The lungs are the point of predilection for the development of tuberculosis.

Delépine[34] used a mixture of various tuberculous sputa, because tubercle cultures are apt to lose in great part their virulence and also because tuberculous material from man varies greatly in virulence. Six different specimens of sputa were obtained from the Manchester Consumption Hospital and thoroughly mixed. Four calves, which had not been tested with tuberculin because of the possibility that tuberculin might prevent the disease, were inoculated one in the lung, one subcutaneously, one intraperitoneally, and one was fed milk containing tuberculous sputum. The following results were reported: Calf No. 1, which received 5 c. c. of sputum mixture in the lung, died on the sixth day and showed on postmortem generalized tuberculosis which could not be referred to the inoculation. Calf No. 2, which received 5 c. c. of the mixture under the skin of the leg, died on the sixth day and showed enlargement of a gland 5 inches from the point of inoculation and no other trace of tuberculosis. Live virulent tubercle bacilli were found in the skin. Calf No. 3 received 50 c. c. of sputum mixture with its food in one day; died on the twenty-sixth day; tuberculosis of the esophageal glands, which contained virulent tubercle bacilli. Calf No. 4 received 5 c. c. of sputum mixture intraperitoneally. Twenty-six days after inoculation did not react to tuberculin; sixty-eight days after inoculation gave typical reaction; killed twenty days later and showed plainly tuberculosis of the peritoneum, spreading also to the pleura and pericardium. In addition, some lymph glands which were in relation with the peritoneum were tuberculous.

In these experiments only two calves lived long enough to give definite results. Both of these calves were affected with tuberculosis—one from feeding and the other from intraperitoneal injection with human tuberculous sputum. It must be admitted that the value of Delépine's work is very seriously affected by the fact that one of his calves died a few days after the beginning of the experiment of a recently developed generalized tuberculosis.

Hamilton and Young[35] for their experiments selected, first, calves varying in age from two days to ten weeks. The stall in which the animals were kept had never been occupied by cattle before. The experimental animals were fed upon milk, some meal, and a small amount of hay. The milk was obtained from cows which had not reacted to tuberculin, and every endeavor was used to avoid infection from the outside.

First experiment: Five calves were fed with milk containing human tuberculous sputum. Four of these animals were killed in from sixty-five to sixty-nine days after the beginning of the feeding and showed tuberculous changes in the retropharyngeal, mediastinal, and neck glands. The tuberculous character of the lesions was demonstrated by the presence of tubercle bacilli and giant cells and by the development of tuberculosis in guinea pigs which were inoculated with tiss
One of the calves died of septicemia thirty- after the be
ning of the experiment.

Second experiment: Four calves wer bcutan
with small fragments of a lymph gla a tuber

human being. Three of these animals were killed in from sixty-six to eighty-seven days after the inoculation. One calf died twenty-two days after the beginning of the experiment. Of the first three, one remained healthy. The second showed tuberculous changes at the point of inoculation, in the neighboring lymph glands, and in the retropharyngeal and mesenteric lymph glands. In the latter case tubercle bacilli were found. In the fourth calf a number of lymph glands were diseased and isolated tuberculous areas were found in the lung. Another calf was inoculated subcutaneously with a fragment of lung taken from a man who had died of miliary tuberculosis. Eighty-seven days after the inoculation the animal was killed and tuberculous changes were noted at the point of inoculation, together with caseation of many lymph glands, and in addition two thickened areas at the base of the left lung. With the caseous material from the bronchial glands guinea pigs were made tuberculous. Finally, another calf was inoculated subcutaneously with urine containing tubercle bacilli which had been obtained from a man. This animal was killed fifty-five days after inoculation and showed enlargement and caseation of the retropharyngeal, mesenteric, and bronchial lymph glands and, in addition, tuberculous areas in the right lung.

Third experiment: Two calves were inoculated subcutaneously with fragments of tuberculous glands from men. In these cases also, when the animals were killed, more or less tuberculosis was found.

A third animal was inoculated subcutaneously with tuberculous sputum. After one hundred and fifty-five days it showed tuberculous bronchial and mesenteric glands. The point of inoculation seemed to be healthy. Two other calves which had been subjected twice to the tuberculin test and had not reacted inhaled tuberculous sputum and showed, one hundred and forty-five days later, marked tuberculosis of the lungs.

Fourth experiment: In order to ascertain what influence the passage of human tubercle bacilli from animal to animal would have upon the virulence of the microorganism, two calves were inoculated subcutaneously with material taken from another calf which had been previously inoculated with human tuberculous sputum. The experiment resulted in emaciation and loss of appetite of the animals. The autopsy showed generalized tuberculosis. As a result of the above experiments the authors reach the following conclusions:

Although the human tubercle bacillus is apparently not so virulent for calves as the bovine bacillus, yet it can infect cattle. The infection may be brought about by means of tuberculous sputum and tuberculous lymph glands or lung tissue. The disease may be brought about through intravenous or subcutaneous inoculations, through inhalation of pulverized sputum containing tubercle bacilli, or through feeding tuberculous sputum. In the case of feeding, the abdominal lymph glands may become infected without visible lesions of the intestinal walls. The passage of the human tubercle bacillus through calves appears to heighten its virulence enormously. The authors, from the above experiments, are of the opinion that the human tubercle bacillus is identical with the bovine bacillus, although somewhat weaker in virulence.

The literature reviewed in the foregoing pages has been selected because of its special bearing upon the experiments we have made. and this review is not to be considered complete. For a fuller discussion of this subject, especially in its relation to public health, the reader is referred to Salmon's[36] report to the American Public Health Association on "Bovine Tuberculosis and Public Health."

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